Connecting via Winsock to STN

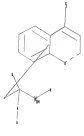
Welcome to STN International! Enter x:x

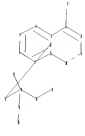
* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:05:20 ON 30 JUL 2009

=> file reg

=>
Uploading C:\Program Files\Stnexp\Queries\3596270.str





chain nodes :
12 13 14 15 17 18 24

```
ring nodes :
1  2  3  4  5  6  7  8  9  10
ring/chain nodes :
16  19
chain bonds :
7-12  13-14  14-15  14-17  14-19  15-16  17-18
ring bonds :
1-2  1-6  1-10  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10
exact/norm bonds :
1-10  7-12  8-9  9-10  14-17  14-19
exact bonds :
13-14  14-15  15-16  17-18
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  6-7  7-8
isolated ring systems :
containing 1 :


G1:H,Cy,Ak

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:CLASS
22:Atom  24:CLASS



L3      STRUCTURE UPLOADED

=>
Uploading C:\Program Files\Stnexp\Queries\4596270.str
```

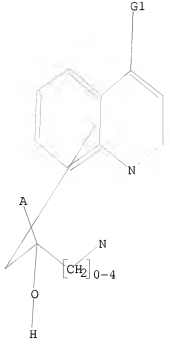
chain nodes :
12 13 14 16 17
ring nodes :
1 2 3 4 5 6 7 8 9 10
ring/chain nodes :
15 18
chain bonds :
7-12 13-18 13-14 13-16 14-15 16-17
ring bonds :
1-2 1-6 1-10 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10
exact/norm bonds :
1-10 7-12 8-9 9-10 13-18 13-16
exact bonds :
13-14 14-15 16-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 6-7 7-8
isolated ring systems :
containing 1 :

G1:H,Cy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 22:Atom

L4 STRUCTURE UPLOADED

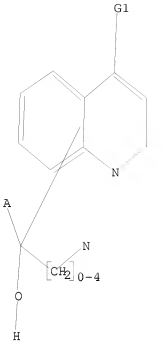
=> d l3
L3 HAS NO ANSWERS
L3 STR



G1 H,Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

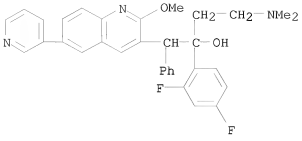
=> d l4
L4 HAS NO ANSWERS
L4 STR



G1 H,Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

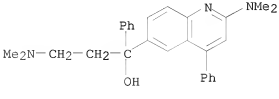
```
=> s l3 sam
SAMPLE SEARCH INITIATED 14:08:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    18897 TO ITERATE

 10.6% PROCESSED     2000 ITERATIONS                                2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:       369707 TO   386173
PROJECTED ANSWERS:             117 TO      637

L5            2 SEA SSS SAM L3

=> d scan

L5   2 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   3-Quinolineethanol, α-(2,4-difluorophenyl)-α-[2-
     (dimethylamino)ethyl]-2-methoxy-β-phenyl-6-(3-pyridinyl)-
MF   C33 H31 F2 N3 O2
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

```
=> s l4 sam
SAMPLE SEARCH INITIATED 14:08:52 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    32448 TO ITERATE

  6.2% PROCESSED     2000 ITERATIONS                                1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       638184 TO   659736
PROJECTED ANSWERS:              83 TO      565

L6            1 SEA SSS SAM L4

=> d scan

L6   1 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   6-Quinolinemethanol, 2-(dimethylamino)-α-[2-(dimethylamino)ethyl]-
     α,4-diphenyl-
MF   C28 H31 N3 O
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

```
=> s l3 or l4 full
FULL SEARCH INITIATED 14:09:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   651448 TO ITERATE

 96.7% PROCESSED   629923 ITERATIONS                              974 ANSWERS

100.0% PROCESSED   651448 ITERATIONS                              974 ANSWERS
SEARCH TIME: 00.00.22

L7          974 SEA SSS FUL L3 OR L4

=> file ca
.

=> s l7
L8          67 L7

=> d ibib abs fhitstr 1-67

L8   ANSWER 1 OF 67  CA  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        151:93317  CA
TITLE:                   A once-weekly R207910-containing regimen exceeds
                         activity of the standard daily regimen in murine
                         tuberculosis
AUTHOR(S):               Veziris, Nicolas; Ibrahim, Murad; Lounis, Nacer;
                         Chauffour, Aurelie; Truffot-Pernot, Chantal; Andries,
                         Koen; Jarlier, Vincent
CORPORATE SOURCE:        Laboratoire de Bacteriologie-Hygiene, Universite
                         Pierre et Marie Curie, Paris, Fr.
SOURCE:                  American Journal of Respiratory and Critical Care
                         Medicine (2009), 179(1), 75-79
                         CODEN: AJCMED; ISSN: 1073-449X
PUBLISHER:               American Thoracic Society
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Rationale: R207910 (TMC207 or J) is a member of the diarylquinolines, a
     new family of antituberculous drugs with high bactericidal activity when
     given daily in the murine model of tuberculosis.  R207910 exhibits a long
     half-life and thus is a good candidate for once-weekly therapy of
     tuberculosis.  Objectives: To study the activity of once-weekly R207910
     monotherapy and combinations of R207910 with other antituberculous agents
     (isoniazid, rifapentine, moxifloxacin, and pyrazinamide).  Methods: The
     established infection model of murine tuberculosis was used.  Colony
     counts were determined in the lungs.  Measurements and Main Results: Eight
     weeks of monotherapy reduced the bacillary load by 3 to 4 log10 for
     rifapentine and by 5 to 6 log10 for R207910 (P < 0.05).  The addition of
     rifapentine and isoniazid or moxifloxacin did not improve the bactericidal
     activity of R207910 monotherapy.  In contrast, the triple combination of
     R207910 plus rifapentine plus pyrazinamide given once weekly for 2 mo
     (i.e., a total of only eight administrations), was significantly (P <
     0.05) more active than R207910 monotherapy or other R207910 combinations,
     and led to lung culture negativity in 9 of 10 mice, whereas all lungs were
     culture pos. in the groups treated with other drug combinations.
     Moreover, R207910 plus rifapentine plus pyrazinamide given once weekly was
     more active than the current standard regimen of rifampin plus isoniazid plus
```

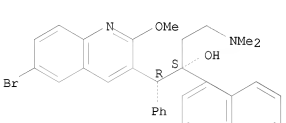
pyrazinamide given five times per wk. Conclusions: The unprecedented activity of the triple combination of R207910 plus rifapentine plus pyrazinamide suggests that it may be feasible to develop a fully intermittent once-weekly regimen.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(once-weekly R207910 alone and in combination with rifapentine plus pyrazinamide showed similar high bactericidal activity which exceeded that of standard daily regimen in mouse model of tuberculosis)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 151:23548 CA

TITLE: ATP synthase and the actions of inhibitors utilized to study its roles in human health, disease, and other scientific areas

AUTHOR(S): Hong, Sangjin; Pedersen, Peter L.

CORPORATE SOURCE: Department of Biological Chemistry, School of Medicine, Johns Hopkins University, Baltimore, MD, 21205-2185, USA

SOURCE: Microbiology and Molecular Biology Reviews (2008), 72(4), 590-641
CODEN: MMBRF7; ISSN: 1092-2172

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. ATP synthase, a double-motor enzyme, plays various roles in the cell, participating not only in ATP synthesis but in ATP hydrolysis-dependent processes and in the regulation of a proton gradient across some membrane-dependent systems. Recent studies of ATP synthase as a potential mol. target for the treatment of some human diseases have displayed promising results, and this enzyme is now emerging as an attractive mol. target for the development of new therapies for a variety of diseases. Significantly, ATP synthase, because of its complex structure, is inhibited by a number of different inhibitors and provides

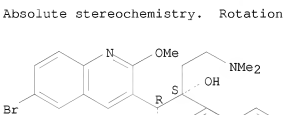
diverse possibilities in the development of new ATP synthase-directed agents. In this review, we classify over 250 natural and synthetic inhibitors of ATP synthase reported to date and present their inhibitory sites and their known or proposed modes of action. The rich source of ATP synthase inhibitors and their known or purported sites of action presented in this review should provide valuable insights into their applications as potential scaffolds for new therapeutics for human and animal diseases as well as for the discovery of new pesticides and herbicides to help protect the world's food supply. Finally, as ATP synthase is now known to consist of two unique nanomotors involved in making ATP from ADP and Pi, the information provided in this review may greatly assist those investigators entering the emerging field of nanotechnol.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ATP synthase inhibitor R207910 as antimycobacterial agent is effective for treatment of tuberculosis in human and animal)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 454 THERE ARE 454 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 150:505896 CA

TITLE: New anti-tuberculosis drugs in clinical trials with novel mechanisms of action

AUTHOR(S): Rivers, Emma C.; Mancera, Ricardo L.

CORPORATE SOURCE: The Open University, Milton Keynes, MK7 6AA, UK

SOURCE: Drug Discovery Today (2008), 13(23/24), 1090-1098
CODEN: DDTOFS; ISSN: 1359-6446

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Tuberculosis is a major health problem worldwide, with approx. 1.7 million people dying annually from the disease. The long current drug regimen, the emergence of drug resistant strains and HIV co-infection have resulted in a resurgence in research efforts to address the urgent need for new anti-tuberculosis drugs. A number of new potential anti-tuberculosis

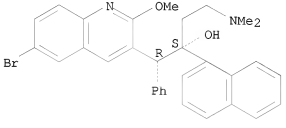
drug candidates with novel modes of action have entered clin. trials in recent years. These agents are most likely to be effective against resistant strains. We provide a concise review of their structure-activity relationships, in vitro and in vivo activity, pharmacokinetics, mechanism of action and combination regimens.

IT 843663-66-1, TMC207
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antituberculosis drug TMC207 with novel mechanism of action and in combination with pyrazinamide showed activity against drug-resistant and susceptible Mycobacterium tuberculosis in patient with tuberculosis)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 150:437841 CA

TITLE: Selectivity of TMC207 towards mycobacterial ATP synthase compared with that towards the eukaryotic homologue

AUTHOR(S): Haagsma, Anna C.; Abdillahi-Ibrahim, Rooda; Wagner, Marijke J.; Krab, Klaas; Vergauwen, Karen; Guillemont, Jerome; Andries, Koen; Lill, Holger; Koul, Anil; Bald, Dirk

CORPORATE SOURCE: Department of Molecular Cell Biology, Faculty of Earth and Life Sciences, VU University Amsterdam, Amsterdam, 1081 HV, Neth.

SOURCE: Antimicrobial Agents and Chemotherapy (2009), 53(3), 1290-1292
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The diarylquinoline TMC207 kills Mycobacterium tuberculosis by specifically inhibiting ATP synthase. We show here that human mitochondrial ATP synthase (50% inhibitory concentration [IC50] of >200 μM) displayed more than 20,000-fold lower sensitivity for TMC207 compared to

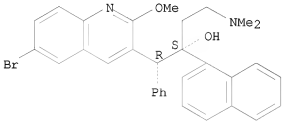
that of mycobacterial ATP synthase (IC50 of 10 nM). Also, oxygen consumption in mouse liver and bovine heart mitochondria showed very low sensitivity for TMC207. These results suggest that TMC207 may not elicit ATP synthesis-related toxicity in mammalian cells. ATP synthase, although highly conserved between prokaryotes and eukaryotes, may still qualify as an attractive antibiotic target.

IT 843663-66-1, TMC207
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ATP synthase inhibition by; selectivity of TMC207 towards mycobacterial ATP synthase compared with that towards human, mouse, or bovine homolog)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 150:413115 CA

TITLE: Structure-Activity Relationships for a Series of Quinoline-Based Compounds Active against Replicating and Nonreplicating Mycobacterium tuberculosis

AUTHOR(S): Lilienkampf, Annamaria; Mao, Jialin; Wan, Baojie; Wang, Yuehong; Franzblau, Scott G.; Kozikowski, Alan P.

CORPORATE SOURCE: Drug Discovery Program, Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612, USA

SOURCE: Journal of Medicinal Chemistry (2009), 52(7), 2109-2118
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tuberculosis (TB) remains as a global pandemic that is aggravated by a lack of health care, the spread of HIV, and the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) strains. New anti-TB drugs are urgently required to shorten the long 6-12 mo treatment regimen and to battle drug-resistant Mtb strains. We have identified several potent quinoline-based anti-TB compds., bearing an isoxazole containing side-chain. The most potent compds., 7g and 13,

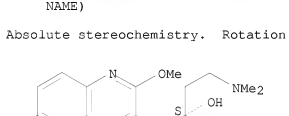
exhibited submicromolar activity against the replicating bacteria (R-TB), with min. inhibitory concns. (MICs) of 0.77 and 0.95 μM, resp. In general, these compds. also had micromolar activity against the nonreplicating persistent bacteria (NRP-TB) and did not show toxicity on Vero cells up to 128 μM concentration Compds. 7g and 13 were shown to retain their anti-TB activity against rifampin, isoniazid, and streptomycin resistant Mtb strains. The results suggest that quinoline-isoxazole-based anti-TB compds. are promising leads for new TB drug development.

IT 843663-66-1, Tmc207
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SAR and preparation of quinoline compds. active against M. tuberculosis)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 150:344009 CA

TITLE: Extracting metabolite ions out of a matrix background by combined mass defect, neutral loss and isotope filtration

AUTHOR(S): Cuyckens, Filip; Hurkmans, Rob; Castro-Perez, Jose M.; Leclercq, Laurent; Mortishire-Smith, Russell J.

CORPORATE SOURCE: Global Preclinical Development, Johnson and Johnson Pharmaceutical R and D, Beerse, 2340, Belg.

SOURCE: Rapid Communications in Mass Spectrometry (2009), 23(2), 327-332
CODEN: RCMSEF; ISSN: 0951-4198

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mass defect, neutral loss and isotope filtration techniques were applied to electrospray ionization mass spectrometry (ESI-MS) data obtained for in vivo and in vitro samples of drug metabolism studies. A combination of these post-acquisition processing techniques was shown to be more powerful than the use of one of these tools alone for the detection in complex matrixes of metabolites of candidate drugs with a characteristic isotope pattern (e.g. containing bromine, chlorine, or a high proportion of radiolabeled drug (12C/14C)) or characteristic neutral losses. In combination with 'all-in-one' data acquisition this methodol. is able to perform software-driven constant neutral loss scanning for an unlimited number of mass

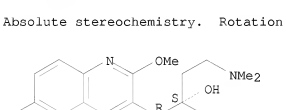
differences at any time after anal. Highly selective MS chromatograms were obtained with excellent correlation with their corresponding radiochromatograms.

IT 843663-66-1, TMC207
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(extracting metabolite ions out of matrix background by combined mass defect, neutral loss and isotope filtration)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	10	THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	150:325707 CA
TITLE:	Prevention of drug carryover effects in studies assessing antimycobacterial efficacy of TMC207
AUTHOR(S):	Lounis, Nacer; Gevers, Tom; Van Den Berg, Joke; Verhaeghe, Tom; van Heeswijk, Rolf; Andries, Koen
CORPORATE SOURCE:	Tibotec BVBA, Johnson and Johnson, Beerse, 2340, Belg.
SOURCE:	Journal of Clinical Microbiology (2008), 46(7), 2212-2215 CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The levels of TMC207 (R207910) that can be reached in mouse organs and the sputa of treated patients easily exceed the MIC of the compound and can therefore interfere with in vitro bacterial titrns. We studied the usefulness of protein-enriched media for the prevention of such drug carryover effects. The average MIC of Mycobacterium tuberculosis was determined on three different media: unsupplemented 7H11 agar (MIC = 0.03 μg/mL), 7H11 agar supplemented with 5% bovine serum albumin (BSA; MIC = 1 μg/mL), and Lowenstein-Jensen medium (MIC = 14.33 μg/mL). In a second stage of the study, the maximal noninhibitory concns. (MNICs) of TMC207 were determined by adding TMC207 to the bacterial inoculum rather than to the culture medium. These MNICs were 0.97 μg/mL for 7H11 agar, 32.33 μg/mL for 7H11 agar with 5% BSA, and 96.33 μg/mL for

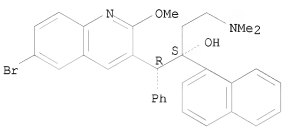
Lowenstein-Jensen medium. Both protein-enriched media were able to prevent drug carryover effects, but the use of 7H11 medium supplemented with 5% BSA is preferred for practical reasons.

IT 843663-66-1, TMC207
RL: BSU (Biological study, unclassified); BIOL (Biological study) (prevention of drug carryover effects in studies assessing antimycobacterial efficacy of TMC207)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 150:320527 CA

TITLE: A roadmap for drug discovery and its translation to small molecule agents in clinical development for tuberculosis treatment

AUTHOR(S): Showalter, H. D. Hollis; Denny, William A.

CORPORATE SOURCE: Department of Medicinal Chemistry, University of Michigan, Ann Arbor, MI, 48109-1965, USA

SOURCE: Tuberculosis (Oxford, United Kingdom) (2008), 88(Suppl. 1), S3-S17
CODEN: TUBECU; ISSN: 1472-9792

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal; General Review

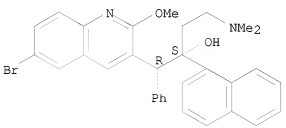
LANGUAGE: English

AB A review. Drug discovery and development, from an initial disease treatment concept to a new drug application (NDA), is a complex, lengthy and expensive process. In this review we discuss the key stages of drug discovery and early development, including target identification and validation, assay development and screening, confirmed hits to leads, lead optimization, and progressing development candidates to an investigational new drug (IND) filing. We also provide particular examples of how this process is beginning to assist in the development of small mol. treatments for tuberculosis, by summarizing the status of the clin. development of several newer classes of drugs. These include the fluoroquinolones, oxazolidinones, diarylquinolines, and nitroimidazo-oxazoles and -oxazines.

IT 843663-66-1, TMC207
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(roadmap for drug discovery and its translation to small mol. agents in clin. development for tuberculosis treatment)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

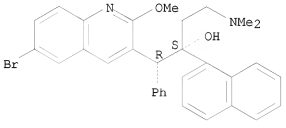


REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 150:159357 CA
TITLE: Design, synthesis and pharmacological evaluation of mefloquine-based ligands as novel antituberculosis agents
AUTHOR(S): Mao, Jialin; Wang, Yuehong; Wan, Baojie; Kozikowski, Alan P.; Franzblau, Scott G.
CORPORATE SOURCE: Institute for Tuberculosis Research University of Illinois, Chicago, USA
SOURCE: CACS Communications (2007), (Fall), 25-26
CODEN: CCAOBD; ISSN: 1939-4004
URL: http://www.cacshq.org/CACS_Fall_2007-FINAL.pdf
PUBLISHER: Chinese-American Chemical Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Mefloquine-based hydrazone analogs were designed and synthesized, and their activity against both replicating and non-replicating persistent tuberculosis (TB) was evaluated using the microplate Alamar Blue assay (MABA) and low oxygen recovery assay (LORA), resp. Clear anti-TB structure-activity relationships (SARs) were observed In addition, the cytotoxicity data toward Vero cells (IC50) and the desired selectivity indexes provided useful information in directing the synthesis. Results confirmed the importance of having a quinoline ring present as the main scaffold, as well as two trifluoromethyl groups to maintain anti-TB activity. For substitution at the remote nitrogen of the piperazine ring, various aliphatic and unsatd. chains are tolerated and a basic terminus is preferred.
IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mefloquine based analog was more active in vero cells and showed reduced mammalian cell toxicity and central nervous system side effects

than mefloquine)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

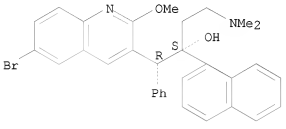
Absolute stereochemistry. Rotation (-).



L8 ANSWER 10 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:508704 CA
TITLE: Diarylquinolines Are Bactericidal for Dormant Mycobacteria as a Result of Disturbed ATP Homeostasis
AUTHOR(S): Koul, Anil; Vranckx, Luc; Dendouga, Najoua; Balemans, Wendy; Van den Wyngaert, Ilse; Vergauwen, Karen; Goehlmann, Hinrich W. H.; Willebrords, Rudy; Poncelet, Alain; Guillemont, Jerome; Bald, Dirk; Andries, Koen
CORPORATE SOURCE: Department of Antimicrobial Research, Johnson & Johnson, Beerse, B-2340, Belg.
SOURCE: Journal of Biological Chemistry (2008), 283(37), 25273-25280
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An estimated one-third of the world population is latently infected with Mycobacterium tuberculosis. These nonreplicating, dormant bacilli are tolerant to conventional antituberculosis drugs, such as isoniazid. We recently identified diarylquinoline R207910 (also called TMC207) as an inhibitor of ATP synthase with a remarkable activity against replicating mycobacteria. In the present study, we show that R207910 kills dormant bacilli as effectively as aerobically grown bacilli with the same target specificity. Despite a transcriptional down-regulation of the ATP synthase operon and significantly lower cellular ATP levels, we show that dormant mycobacteria do possess residual ATP synthase enzymic activity. This activity is blocked by nanomolar concns. of R207910, thereby further reducing ATP levels and causing a pronounced bactericidal effect. We conclude that this residual ATP synthase activity is indispensable for the survival of dormant mycobacteria, making it a promising drug target to tackle dormant infections. The unique dual bactericidal activity of diarylquinolines on dormant as well as replicating bacterial subpopulations distinguishes them entirely from the current anti-tuberculosis drugs and underlines the potential of R207910 to shorten tuberculosis treatment.
IT 843663-66-1D, R207910, analogs

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diarylquinolines are bactericidal for dormant mycobacteria as a result of disturbed ATP homeostasis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:466203 CA
TITLE: The protonmotive force is required for maintaining ATP homeostasis and viability of hypoxic, nonreplicating Mycobacterium tuberculosis
AUTHOR(S): Rao, Srinivasa P. S.; Alonso, Sylvie; Rand, Lucinda; Dick, Thomas; Pethe, Kevin
CORPORATE SOURCE: Novartis Institute for Tropical Diseases, Chromos, 138670, Singapore
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2008), 105(33), 11945-11950 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The persistence of Mycobacterium tuberculosis despite prolonged chemotherapy represents a major obstacle for the control of tuberculosis. The mechanisms used by Mtb to persist in a quiescent state are largely unknown. Chemical genetic and genetic approaches were used here to study the physiol. of hypoxic nonreplicating mycobacteria. We found that the intracellular concentration of ATP is five to six times lower in hypoxic nonreplicating Mtb cells compared with aerobic replicating bacteria, making them exquisitely sensitive to any further depletion. We show that de novo ATP synthesis is essential for the viability of hypoxic nonreplicating mycobacteria, requiring the cytoplasmic membrane to be fully energized. In addition, the anaerobic electron transport chain was demonstrated to be necessary for the generation of the protonmotive force. Surprisingly, the alternate ndh-2, but not -1, was shown to be the electron donor to the electron transport chain and to be essential to replenish the [NAD+] pool in hypoxic nonreplicating Mtb. Finally, we

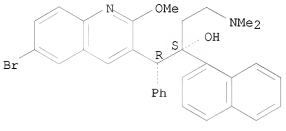
describe here the high bactericidal activity of the F0F1 ATP synthase inhibitor R207910 on hypoxic nonreplicating bacteria, supporting the potential of this drug candidate for shortening the time of tuberculosis therapy.

IT 843663-66-1, R207910
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high bactericidal activity of F0F1 ATP synthase inhibitor R207910 on hypoxic nonreplicating bacteria)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:439060 CA
TITLE: Handbook of anti-tuberculosis agents
AUTHOR(S): Anon.
CORPORATE SOURCE: Global Alliance for TB Drug Development, New York, NY, 10004, USA
SOURCE: Tuberculosis (Oxford, United Kingdom) (2008), 88(2), 85-170
CODEN: TUBECU; ISSN: 1472-9792
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

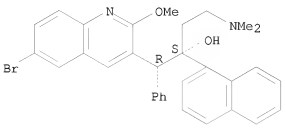
AB A review on information on all approved drugs used to treat tuberculosis (TB), on drugs in clin. development for TB, and on some approved drugs being investigated for potential use in TB.

IT 843663-66-1, TMC-207
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TMC-207 may useful as antituberculosis agent for potential use in patient with tuberculosis)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

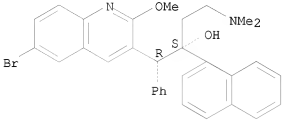
L8 ANSWER 13 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:369690 CA
TITLE: Impact of the interaction of R207910 with rifampin on the treatment of tuberculosis studied in the mouse model
AUTHOR(S): Lounis, Nacer; Gevers, Tom; Van Den Berg, Joke; Andries, Koen
CORPORATE SOURCE: Department of Antimicrobial Research, Tibotec BVBA, Johnson and Johnson, Beerse, 2340, Belg.
SOURCE: Antimicrobial Agents and Chemotherapy (2008), 52(10), 3568-3572
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New drugs are needed to shorten the duration of tuberculosis treatment. R207910, a diarylquinoline, is very active against Mycobacterium tuberculosis both in vitro and in mice. In healthy volunteers, the coadministration of R207910 and rifampin induced the increased metabolism of R207910, resulting in a 50% reduction in the level or R207910 exposure. We assessed the impact of reducing the dose of R207910 on its efficacy when R207910 was combined with a background regimen of isoniazid, rifampin, and pyrazinamide. Addition of 25 mg/kg of body weight or 12.5 mg/kg R207910 to the background regimen resulted in faster bacterial clearance and culture negativity. The difference in efficacy between the two doses was not statistically significant. The minimal bactericidal dose of R207910 when it was tested as part of the combination was identical to that when it was tested as monotherapy. Because of the drug-drug interaction in humans, the activity of R207910 in humans could be less than that expected from studies with mice. Our data from the mouse model demonstrate that R207910 has significant activity, even when its exposure is reduced by 50% and when it is added to a strong background regimen of isoniazid, rifampin, and pyrazinamide. In killing kinetic studies, the bactericidal effect of R207910 in mice was modest during the first week of treatment, but it increased in the following 3 wk, while the bactericidal activity of isoniazid was limited to the first week of treatment.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of interaction of R207910 with rifampin on treatment of tuberculosis studied in mouse model)

RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

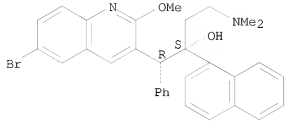
Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:238540 CA
TITLE: Novel treatment strategies for TB patients with HIV co-infection
AUTHOR(S): Ginsberg, Ann M.
CORPORATE SOURCE: Clinical Development, Global Alliance for Tuberculosis Drug Development, New York, NY, 10004, USA
SOURCE: Handbook of Tuberculosis: Clinics, Diagnostics, Therapy and Epidemiology (2008), 213-225. Editor(s): Kaufmann, Stefan H. E.; van Helden, Paul. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany. CODEN: 69KWLS; ISBN: 978-3-527-31888-9
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review on the goals and approaches for improving tuberculosis treatment of patients co-infected with HIV, as well as the drugs in clin. development for a TB indication and their interactions with the cytochrome P 450 enzymes.
IT 843663-66-1, TMC207
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TMC207 in combination with antiretroviral agent showed no cytochrome P 450 interaction and may be effective in treating tuberculosis patient with human immunodeficiency virus co-infection)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

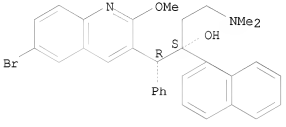


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:215199 CA
TITLE: Early bactericidal activity and pharmacokinetics of the diarylquinoline TMC207 in treatment of pulmonary tuberculosis
AUTHOR(S): Rustomjee, R.; Diacon, A. H.; Allen, J.; Venter, A.; Reddy, C.; Patientia, R. F.; Mthiyane, T. C. P.; De Marez, T.; van Heeswijk, R.; Kerstens, R.; Koul, A.; De Beule, K.; Donald, P. R.; McNeeley, D. F.
CORPORATE SOURCE: Unit for Clinical and Biomedical Tuberculosis Research, Medical Research Council, Durban, S. Afr.
SOURCE: Antimicrobial Agents and Chemotherapy (2008), 52(8), 2831-2835
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tibotec Medicinal Compound 207 (TMC207) is a novel diarylquinoline with a unique mode of action that targets mycobacterial ATP synthase. TMC207 exhibits high in vitro activity against mycobacterial strains either susceptible or resistant to all first-line and many second-line drugs, including fluoroquinolones, and has shown exceptional in vivo activity against several mycobacterial species in different animal models. In this early bactericidal activity study, 75 treatment-naive patients with smear-pos. pulmonary tuberculosis were randomized to once-daily oral TMC207 (25 mg, 100 mg, or 400 mg), 600 mg rifampin (RIF), or 300 mg isoniazid (INH) for 7 days. Sixteen-hour overnight sputum collected at baseline and on each treatment day was plated in serial dilns. on selective agar plates. The bactericidal activity was expressed as the log10 decrease in CFU/mL sputum/day. Pharmacokinetic sampling was performed on day 7 of TMC207 administration up to 24 h postdose. The decreases in log10 CFU counts (± standard deviation) from baseline to day 7 were 0.04 ± 0.46 for 25 mg TMC207 (n = 14), 0.26 ± 0.64 for 100 mg TMC207 (n = 14), 0.77 ± 0.58 for 400 mg TMC207 (n = 14), 1.88 ± 0.74 for INH (n = 11), and 1.70 ± 0.71 for RIF (n = 14). Significant bactericidal activity of 400 mg TMC207 was observed from day 4 onward and was similar in magnitude to those of INH and RIF over the same period. The pharmacokinetics of TMC207 were linear across the dose range. In summary, TMC207 demonstrated bactericidal activity with a delayed onset and was well tolerated, and no study drug-related serious adverse events occurred.
IT 843663-66-1, TMC207
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological

activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(early bactericidal activity and pharmacokinetics of diarylquinoline TMC207 in treatment of pulmonary tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

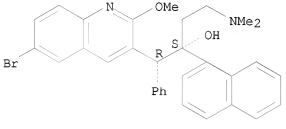


OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:98079 CA
TITLE: ATP synthases: bioinformatic based insights into how their electrochemically driven motor comprised of subunits a and c might serve as a drug target
AUTHOR(S): Maeda, Masatomo
CORPORATE SOURCE: Department of Molecular Biology, School of Pharmaceutical Sciences, Iwate Medical University, Shiwa, Iwate, 028-3694, Japan
SOURCE: Journal of Bioenergetics and Biomembranes (2008), 40(2), 117-121
CODEN: JBBID4; ISSN: 0145-479X
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB F0F1-ATP synthases, widely distributed in bacteria, eukaryotic mitochondria, and chloroplasts, are highly conserved multi-subunit complexes. Although the conserved acidic residue in the transmembrane helix of the c subunit functions in H+ transport, the surrounding residues differ among species. Such divergence could lead to different regulatory modes since pH-dependent H+ transport has been demonstrated in Escherichia coli with a c subunit carrying an addnl. acidic residue in the helix. There is further divergence in the number of c subunits that form the ring structure which is determined by the higher ordered structure. Recently, it was suggested that certain compds. such as R 207910 and mefloquine recognize the a and c subunits of pathogenic bacterial F0 sector. Since there may be structural divergence even in well-conserved ATP synthases, the c subunit-ring as well as the a subunit in F0 could be targets for drugs for specific bacterial species.
IT 843663-66-1, R 207910

RL: BSU (Biological study, unclassified); BIOL (Biological study) (bioinformatic based insights into how the ATP synthase electrochem. driven motor comprised of subunits a and c might serve as a drug target for pathogenic bacteria)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:69158 CA
TITLE: Medications for extensively drug-resistant tuberculosis: back to the future?
AUTHOR(S): Ashby, Charles R., Jr.; Jodlowski, Tomasz Z.; Sym, Donna
CORPORATE SOURCE: ST. John's University College of Pharmacy and Allied Health Professions, Queens, NY, USA
SOURCE: Journal of Pharmacy Technology (2008), 24(2), 82-95 CODEN: JPTEEB; ISSN: 8755-1225
PUBLISHER: Harvey Whitney Books Co.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Objective: To reexamine the existing medications for the potential treatment of extensively drug-resistant tuberculosis (XDR-TB), based on susceptibility data, and to identify potential future medications from the literature. Data Sources: Relevant information was identified through a search of MEDLINE (1966-Nov. 2007), PubMed (1955-Nov. 2007), American Search Premier (1975-Nov. 2007), International Pharmaceutical (1960-Nov. 2007), Science Citation Index Expanded (1996-Nov. 2007), Cochrane Databases (publications archived until Nov. 2007), and various tertiary sources as listed in the refs., using the terms extensively drug-resistant tuberculosis (XDR-TB), ethambutol, pyrazinamide, para-aminosalicylic acid, cycloserine, linezolid, diarylquinoline, nitroimidazopyran, fluoroquinolones, β-lactams, new treatments, and ethionamide alone or in combination regimens. Study Selection and Data Extraction: After identification of the relevant information, the data presented in this article were selected based on clin. relevance and value of information. Data Synthesis: Based on susceptibility data, pyrazinamide, ethambutol, para-aminosalicylic acid, cycloserine, and ethionamide may be used for the treatment of tuberculosis. However, due to the emergence of XDR-TB, many of these agents are no longer successful

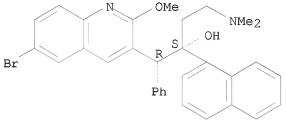
treatment regimens. We have found limited data supporting potential future use of β-lactams, clarithromycin, and linezolid in resistant TB infections. TMC207, nitroimidazopyran, and SQ109 compds. may also prove to be viable options in the near future for treatment of tuberculosis, especially in cases with resistance to mainstay medications. Conclusions: Extensively resistant tuberculosis appears to be a potentially catastrophic disease if allowed to spread. Due to its resistance profile, very few potentially effective agents are available, calling attention to this growing problem.

IT 843663-66-1, TMC207
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TMC207 can be viable option for treatment of patient with extensively drug-resistant tuberculosis)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 189 THERE ARE 189 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 149:53892 CA

TITLE: Preparation of aminohydroxyalkylquinolines as antibacterials.

INVENTOR(S): Guillemont, Jerome Emile Georges; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 64pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068270	A1	20080612	WO 2007-EP63316	20071204

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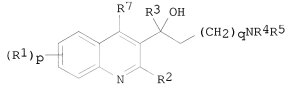
IN 2009MN01241 A 20090717 IN 2009-MN1241 20090701
PRIORITY APPLN. INFO.: EP 2006-125529 A 20061206
WO 2007-EP63316 W 20071204
OTHER SOURCE(S): MARPAT 149:53892
GI



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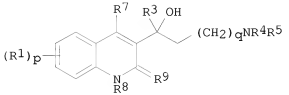

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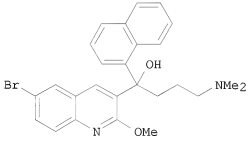


III

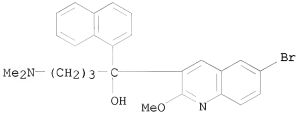
AB Title compds. [I, II; p = 1-4; q = 0-4; R1 = H, cyano, CHO, CO2H, halo, alkyl, alkenyl, alkynyl OH, amino, (substituted) aralkyl, arylcarbonyl, heterocyclyl, etc.; R2 = H, OH, SH, alkoxy, (substituted) aryl, aryloxy, pyrrolidino, piperidinyl, morpholinyl, piperazinyl, etc.; R3 = alkyl, (substituted) aralkyl, aryloxyalkyl aryl, diaryl heterocyclyl, 4-phenylcarbonylpiperidinyl, etc.; R4, R5 = H, alkyl, alkoxyalkyl, (substituted) aralkyl, aryl, heterocyclyl, C(:NH)NH2, etc.; NR4R5 = pyrrolidino, piperidino, piperazino, morpholino, etc.; R7 = H, halo, alkyl, (substituted) aryl, heterocyclyl; R8 = H, alkyl; R9 = O; R8R9 = CH:CHN], were prepared Thus, a mixture prepared from BuLi and 2,2,6,6-tetramethylpiperidine in THF at -70° was treated with 6-bromo-2-methoxyquinoline (preparation given) in THF and then with

1-(5-dimethylaminopentanoyl)naphthalene in THF to give 20% title compound (III). III showed an IC90 value of 7.60 μg/mL against Staphylococcus aureus ATCC 29213.

IT 1032187-20-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminohydroxyalkylquinolines as antibacterials)

RN 1032187-20-4 CA

CN 3-Quinolinemethanol, 6-bromo-α-[3-(dimethylamino)propyl]-2-methoxy-α-1-naphthalenyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 149:53890 CA

TITLE: Antibacterial quinoline derivatives and their preparation and use in the treatment of bacterial infection

INVENTOR(S): Guillemont, Jerome Emile Georges; Motte, Magali Madeleine Simone; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

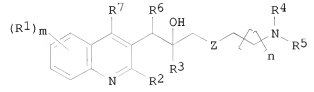
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068269	A1	20080612	WO 2007-EP63315	20071204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-125521 A 20061206

OTHER SOURCE(S): MARPAT 149:53890
GI



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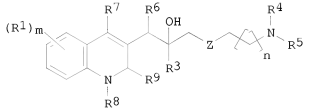
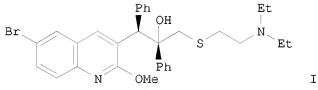


II

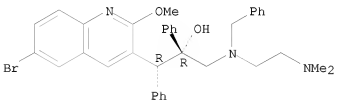


III

AB The invention relates to substituted quinoline derivs. according to the general formula I or II: including any stereochem. isomeric form thereof, a pharmaceutically acceptable salt thereof, a N-oxide form thereof or a solvate thereof. The claimed compds. are useful for the treatment of a bacterial infection. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds., the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of a bacterial infection and a process for preparing the claimed compds. Compds. of formula I and II wherein m is 1, 2, 3, and 4; n is 0, 1, 2, 3 and 4; R1 is H, CN, CHO, carboxyl, halo, (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; R2 is H, alkyloxy, aryl, aryloxy, OH, mercapto, etc.; R3 is alkyl, arylalkyl, aryloxyalkyl, arylalkyloxylakyl, aryl, etc.; R4 and R5 are independently H, alkyl, alkoxyalkyl, arylalkyl, (di)alkylamino, etc.; NRR5aken together to form pyrrolidino piperidino, piperazino, morpholino, thiomorpholino, etc.; R6 is (un)substituted Ph, (un)substituted naphthyl, (un)substituted acenaphthyl (un)substituted tetrahydronaphthyl, and (un)substituted (mono/bi)cyclic heterocycle; R7 is H, halo, alkyl, aryl and (un)substituted (mono/bi)cyclic heterocycle; R8 is H and alkyl; R9 is oxo; R8R9 taken together to form CH=CH-N=; Z is S and NH and derivs.; and their stereochem. isomeric forms, N-oxides, pharmaceutically acceptable salts, and solvates thereof, are claimed. Example compound III was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their antibacterial activity

(data given).
IT 1032015-83-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infection)
RN 1032015-83-0 CA
CN 3-Quinolineethanol, 6-bromo-α-[[[2-(dimethylamino)ethyl](phenylmethyl)amino]methyl]-2-methoxy-α,β-diphenyl-, (αR,βR)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:53889 CA
TITLE: Antibacterial quinoline derivatives and their preparation, and use in the treatment of bacterial infection
INVENTOR(S): Guillemont, Jerome Emile Georges; Dorange, Ismet; Lancois, David Francis Alain; Villalgordo-Soto, Jose Manuel; Simonnet, Yvan Rene Ferdinand; Motte, Magali Madeleine Simone; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 134pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068272	A2	20080612	WO 2007-EP63319	20071204
WO 2008068272	A3	20080724		

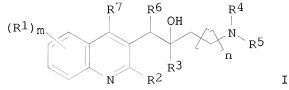
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

CA 2668558	A1	20080612	CA 2007-2668558	20071204
IN 2009MN01242	A	20090717	IN 2009-MN1242	20090701
PRIORITY APPLN. INFO.:			EP 2006-125545	A 20061206
			WO 2007-EP63319	W 20071204

OTHER SOURCE(S): MARPAT 149:53889

GI



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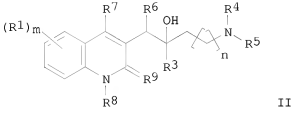

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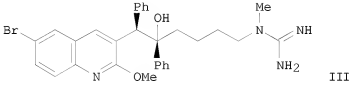


III

AB The invention relates to substituted quinoline derivs. according to the general formula I and II: including any stereochem. isomeric form thereof, a pharmaceutically acceptable salt thereof, a N-oxide form thereof or a solvate thereof. The claimed compds. are useful for the treatment of a bacterial infection. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds., the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of a bacterial infection and a process for preparing the claimed compds. Compds. of formula I and II wherein m is 1, 2, 3 and 4; n is 0, 1, 2, 3 and 4; R1 is H, CN, CHO, carboxy, halo, (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, OH, alkyloxy, etc.; R2 is H, alkyloxy, aryl, aryloxy, OH, mercapto, alkyloxyalkyloxy, etc.; R3 is alkyl, arylalkyl, aryloxyalkyl, arylalkyloxylalkyl, aryl, etc.; R4 is H and alkyl; R5 is C(=NH)NH2, arylalkyl, heterocyclyl-alkyl, (di)alkylaminoalkyl, aryl, etc.; NR4R5 taken together to form azetidinyl, dihydroisoindolyl, thiazolidinyl, etc.; R6 is (un)substituted Ph, (un)substituted naphthyl, (un)substituted

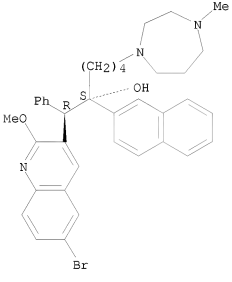
acenaphthyl and (un)substituted tetrahydronaphthyl, etc.; R7 is H, halo, alkyl, aryl, and heterocycle; R8 is H and alkyl; R9 is oxo; R8R9 is CH=CH-N=; and their stereochem. isomeric forms, N-oxides, pharmaceutically acceptable salts and solvates thereof, are claimed. Example compound III was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their antibacterial activity (data given).

IT 1032444-90-8P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate and intermediate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infection)

RN 1032444-90-8 CA

CN 3-Quinolineethanol, 6-bromo-α-[4-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)butyl]-2-methoxy-α-2-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 21 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 149:53888 CA

TITLE: Antibacterial quinoline derivatives and their preparation, and use in the treatment of bacterial infection

INVENTOR(S): Guillemont, Jerome Emile Georges; Lancois, David Francis Alain; Dorange, Ismet; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 96pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068267	A1	20080612	WO 2007-EP63313	20071204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
PRIORITY APPLN. INFO.:			EP 2006-125499	A 20061206
OTHER SOURCE(S):	MARPAT 149:53888			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to substituted quinoline derivs. according to the general formula I and II: including any stereochem. isomeric form thereof, a pharmaceutically acceptable salt thereof, a N-oxide form thereof or a solvate thereof. The claimed compds. are useful for the treatment of a bacterial infection. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds., the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of a bacterial infection and a process for preparing the claimed compds. Compds. of formula I and II wherein m is 1, 2, 3 and 4; n is 0, 1, 2, 3 and 4; R1 is alkenyl, alkynyl, C-NOH and derivs., amino, (di)alkylamino, aminoalkyl, etc.; R2 is H, alkyloxy, aryl, aryloxy, OH, mercapto, alkyloxyalkyloxy, etc.; R3 is alkyl, arylalkyl, aryloxyalkyl, arylalkyloxylalkyl, aryl, etc.; R4 and R5 are independently H, alkyl and Bn; NR4R5 taken together to form pyrrolidinyl, pyrrolyl, imidazolinyl, etc.; R6 is (un)substituted Ph, (un)substituted naphthyl, (un)substituted acenaphthyl and (un)substituted tetrahydronaphthyl, etc.; R7 is H, halo, alkyl, aryl, and heterocycle; R8 is H and alkyl; R9 is oxo; R8R9 is CH=CH-N=; and their stereochem. isomeric forms, N-oxides, pharmaceutically acceptable salts and solvates thereof, are claimed. Example compound III was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their antibacterial activity (data given).

IT 1032265-28-3P

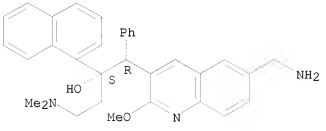
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate and intermediate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infection)

RN 1032265-28-3 CA

CN 3-Quinolineethanol, 6-(aminomethyl)-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αR,βS)-rel-
(CA INDEX NAME)

Relative stereochemistry.



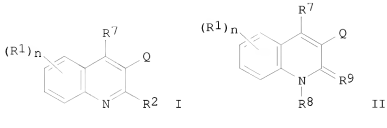
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:53887 CA
TITLE: Antibacterial quinoline derivatives and their preparation and use in the treatment of bacterial infection
INVENTOR(S): Guillemont, Jerome Emile Georges; Dorange, Ismet; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

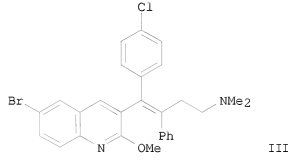
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068266	A1	20080612	WO 2007-EP63312	20071204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-125546 A 20061206
OTHER SOURCE(S): MARPAT 149:53887
GI



I II



III

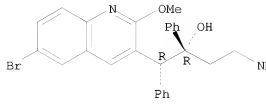
AB The invention relates to substituted quinoline derivs. according to the general formula I and II: including any stereochem. isomeric form thereof, N-oxide thereof, a pharmaceutically acceptable salt thereof or a solvate thereof. The claimed compds. are useful for the treatment of a bacterial infection. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds., the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of a bacterial infection and a process for preparing the claimed compds. Compds. of formula I and II wherein Q is substituted aminoalk-1-enyl, substituted aminoalk-2-enyl, substituted 2-(aminoalkyl)alk-2-enyl; n is 1, 2, 3 and 4; R1 is H, CN, CHO, CO, halo, (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, OH, alkoxy, etc.; R2 is H, alkoxy, aryl, aryloxy, OH, mercapto, , etc.; R7 is H, halo, alkyl, aryl, and monocyclic heterocycle; R8 is H and alkyl; R9 is oxo; R8R9 taken together to form CH=CH-N=; and their stereochem. isomeric forms, N-oxides, pharmaceutically acceptable salts, and solvates thereof, are claimed. Example compound III was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their antibacterial activity. From the assay, it was determined that compound III exhibited IC90 value of 1.65 μG/mL.

IT 654653-58-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infection)

RN 654653-58-4 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α,β-diphenyl-, (αR,βR)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:53885 CA
TITLE: Antibacterial quinoline derivatives and their preparation, and use in the treatment of bacterial infection
INVENTOR(S): Guillemont, Jerome Emile Georges; Dorange, Ismet; Motte, Magali Madeleine Simone; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068268	A1	20080612	WO 2007-EP63314	20071204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-125510 A 20061206
OTHER SOURCE(S): MARPAT 149:53885
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to substituted quinoline derivs. according to the general formula I and II: including any stereochem. isomeric form thereof, a pharmaceutically acceptable salt thereof, a N-oxide form thereof or a solvate thereof. The claimed compds. are useful for the treatment of a

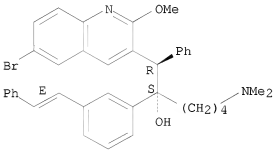
bacterial infection. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds., the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of a bacterial infection and a process for preparing the claimed compds. Compds. of formula I and II wherein m is 1, 2, 3 and 4; n is 0, 1, 2, 3 and 4; R1 is H, CN, CHO, carboxy, halo, (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, OH, alkyloxy, etc.; R2 is H, alkyloxy, aryl, aryloxy, OH, mercapto, alkyloxyalkyloxy, etc.; R3 is alkyl, arylalkyl, aryloxyalkyl, arylalkyloxylalkyl, aryl, etc.; R4 and R5 are independently is H, alkyl and Bn; NR4R5 taken together to form pyrrolidinyl, pyrrolyl, imidazolidinyl, etc.; R6 is (un)substituted Ph, (un)substituted naphthyl, (un)substituted acenaphthyl and (un)substituted tetrahydronaphthyl, etc.; R7 is H, halo, alkyl, aryl, and heterocycle; R8 is H and alkyl; R9 is oxo; R8R9 is CH=CH-N=; and their stereochem. isomeric forms, N-oxides, pharmaceutically acceptable salts and solvates thereof, are claimed. Example compound III was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their antibacterial activity (data given).

IT 1032357-03-1P
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug candidate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infection)

RN 1032357-03-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[4-(dimethylamino)butyl]-2-methoxy-β-phenyl-α-[3-[(1E)-2-phenylethenyl]phenyl]-, (αR,βS)-rel- (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 149:38832 CA
TITLE: Fumarate salt of (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-alpha-1-naphthalenyl-β-phenyl-3-quinoline-ethanol for treatment of a mycobacterial infection
INVENTOR(S): Hegyi, Jean Francois Alexandre Lucas; Aelterman, Wim

Albert Alex; Lang, Yolande Lydia; Maria Stokbroekx, Sigrid Carl; Leys, Carina; Maria Van Remoortere, Peter Jozef; Faure, Anne
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 24pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

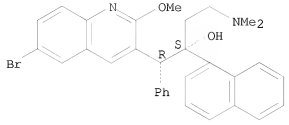
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008068231	A1	20080612	WO 2007-EP63186	20071203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: EP 2006-125443 A 20061205
OTHER SOURCE(S): CASREACT 149:38832

AB The present invention relates to the fumarate salt of (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-alpha-1-naphthalenyl-β-phenyl-3-quinoline-ethanol, pharmaceutical compns. comprising as active ingredient said salt, processes for their preparation and use to treat or prevent a mycobacterial infection. Thus, the reaction of 10 g (0.018 mol) of (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-3-quinoline-ethanol with 2.13 g (0.018 mol) of fumaric acid in isopropanol yielded 10 g (82%) of (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-alpha-1-naphthalenyl-β-phenyl-3-quinoline-ethanol (2E)-2-butenedioate (1:1). A tablet composition contained the fumarate salt 120.89 mg (100 mg base equivalent), lactose monohydrate 152.91 mg, maize starch 66 mg, hypromellose 8 mg, Polysorbate 20 1 mg, microcryst. cellulose 82.2 mg, Croscarmellose sodium 23 mg, colloidal silica 1.4 mg, and magnesium stearate 4.6 mg. Tablets obtained may further optionally be film coated with an aqueous suspension of Opadry II White.

IT 843663-66-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and solid oral compns. of fumarate salt of (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-3-quinoline-ethanol for prevention and treatment of mycobacterial infection)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

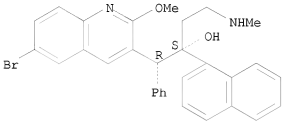


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:569305 CA
TITLE: Use of the bromine isotope ratio in HPLC-ICP-MS and HPLC-ESI-MS analysis of a new drug in development
AUTHOR(S): Cuyckens, Filip; Balcaen, Lieve I. L.; Wolf, Kenny; Samber, Bjorn; Looveren, Cis; Hurkmans, Rob; Vanhaecke, Frank
CORPORATE SOURCE: Global Preclinical Development, Johnson & Johnson Pharmaceutical R&D, Beerse, 2340, Belg.
SOURCE: Analytical and Bioanalytical Chemistry (2008), 390(7), 1717-1729
CODEN: ABCNBP; ISSN: 1618-2642
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A combination of inductively coupled plasma mass spectrometry (ICP-MS) and electrospray ionization mass spectrometry (ESI-MS) was deployed for the metabolite profiling and metabolite identification of a new antituberculosis compound (R207910, also known as TMC207) that is currently in drug development. R207910 contains one bromine atom, allowing the detection by ICP-MS. Fluctuations in the Br sensitivity caused by the HPLC gradient were counteracted by the use of species-unspecific isotope dilution In order to evaluate the method developed, the results obtained were compared with those acquired via radioactivity detection. HPLC-ESI-MS was used for the structural identification of R207910 and its metabolites. The 79Br/81Br isotope ratio is also valuable in the search for metabolites in the complex background of endogenous compds. obtained using HPLC-ESI-MS analyses. Data-dependent scanning using isotope recognition with an ion trap mass spectrometer or processing of Q-Tof data provides HPLC-ICP-MS-like "bromatograms". The combination of accurate mass measurements and the fragmentation behavior in the MS2 spectra obtained using the Q-Tof Ultima mass spectrometer or MSn spectra acquired using the LTQ-Orbitrap allowed structural characterization of the main metabolites of R207910 in methanolic dog and rat feces exts. taken 0-24 h post-dose.
IT 861709-47-9
RL: ANT (Analyte); BSU (Biological study, unclassified); FMU (Formation, unclassified); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(use of bromine isotope ratio in HPLC-ICP-MS and HPLC-ESI-MS anal. of new drug in development)
RN 861709-47-9 CA

CN 3-Quinolineethanol, 6-bromo-2-methoxy-α-[2-(methylamino)ethyl]-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

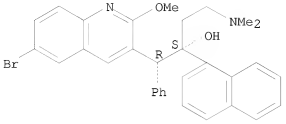
Absolute stereochemistry.



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 148:4856 CA
TITLE: In vitro antimycobacterial spectrum of a diarylquinoline ATP synthase inhibitor
AUTHOR(S): Huitric, Emma; Verhasselt, Peter; Andries, Koen; Hoffner, Sven E.
CORPORATE SOURCE: Swedish Institute for Infectious Disease Control, Solna, Swed.
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(11), 4202-4204
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The diarylquinoline R207910 is in clin. development for tuberculosis treatment. The MIC50 for 41 drug-susceptible and 44 multidrug-resistant Mycobacterium tuberculosis clin. isolates was 0.032 μg/mL. Out of 20 addnl. mycobacterial species, 3 were found to be naturally resistant to R207910 and were shown to exhibit a polymorphism in their atpE genes.
IT 843663-66-1, R207910
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimycobacterial activity of diarylquinoline ATP synthase inhibitor R207910 against drug-susceptible and multidrug-resistant Mycobacterium tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



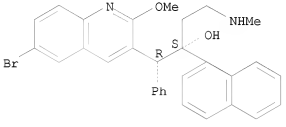
OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:495951 CA
TITLE: Hyphenation of reverse-phase HPLC and ICP-MS for metabolite profiling-application to a novel antituberculosis compound as a case study
AUTHOR(S): Balcaen, Lieve I. L.; Samber, Bjoern; Wolf, Kenny; Cuyckens, Filip; Vanhaecke, Frank
CORPORATE SOURCE: Department of Analytical Chemistry, Ghent University, Ghent, 9000, Belg.
SOURCE: Analytical and Bioanalytical Chemistry (2007), 389(3), 777-786
CODEN: ABCNBP; ISSN: 1618-2642
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, a high-performance liquid chromatog. (HPLC) inductively coupled plasma (ICP) mass spectrometry (MS) method was developed intended for use in metabolism studies of bromine-containing drugs, administered to test animals (or test persons). As a case study, the method was applied to a new antituberculosis compound, the bromine-containing diarylquinoline R207910. A method was proposed to overcome the incompatibilities between the high organic solvent content (45% CH3OH and 45% CH3CN) used in the reverse-phase liquid chromatog. (LC) separation on one hand and the limitations of the ICP on the other hand. Therefore, several instrument modifications had to be made. For the introduction of the column effluent, a combination of a perfluoroalkoxy LC nebulizer with a PC3 Peltier-cooled inlet system (operated at 2 °C) was used. Addnl., the standard injector tube (internal diameter 2 mm) was replaced by an injector tube with an internal diameter of 1 mm and to avoid carbon build-up on the interface cones and the torch, the nebulizer gas was admixed with 6% volume/volume of oxygen. After optimization of the method, HPLC-ICP-MS was applied for metabolite profiling of feces samples after dosing of 14C-radiolabeled R207910 to dogs and rats. To evaluate the method developed, the HPLC-ICP-MS results were compared with those of HPLC with UV spectrophotometric and 14C radiochem. detection. As the HPLC-ICP-MS method gave rise to a higher selectivity than HPLC with UV detection and to a better detection limit (5 ng R207910) than the method with radiochem. detection (65 ng R207910), it can be concluded that ICP-MS can be used as a good alternative to the more traditional detection methods, even when a mobile phase with high organic solvent content has to be used in the LC separation

IT 861709-47-9, R 207910m
RL: ANT (Analyte); ANST (Analytical study)
(hyphenated RP-HPLC-ICP-MS method for metabolite profiling of novel antituberculosis compound)
RN 861709-47-9 CA
CN 3-Quinolineethanol, 6-bromo-2-methoxy-α-[2-(methylamino)ethyl]-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:291461 CA
TITLE: Location of persisting mycobacteria in a guinea pig model of tuberculosis revealed by R207910
AUTHOR(S): Lenaerts, Anne J.; Hoff, Donald; Aly, Sahar; Ehlers, Stefan; Andries, Koen; Cantarero, Luis; Orme, Ian M.; Basaraba, Randall J.
CORPORATE SOURCE: Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, CO, 80523, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(9), 3338-3345
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The lengthy chemotherapy of tuberculosis reflects the ability of a small subpopulation of Mycobacterium tuberculosis bacteria to persist in infected individuals. To date, the exact location of these persisting bacteria is not known. Lung lesions in guinea pigs infected with M. tuberculosis have striking similarities, such as necrosis, mineralization, and hypoxia, to natural infections in humans. Guinea pigs develop necrotic primary lesions after aerosol infection that differ in their morphol. compared to secondary lesions resulting from hematogenous dissemination. In infected guinea pigs conventional therapy for tuberculosis during 6 wk reduced the bacterial load by 1.7 logs in the lungs and, although this completely reversed lung inflammation associated with secondary lesions, the primary granulomas remained largely unaffected. Treatment of animals with the exptl. drug R207910 (TMC207) for 6 wk was highly effective with almost complete eradication of the

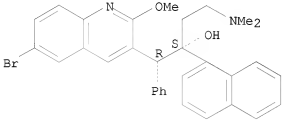
bacteria throughout both the primary and the secondary lesions. Most importantly, the few remnants of acid-fast bacilli remaining after R207910 treatment were to be found extracellular, in a microenvironment of residual primary lesion necrosis with incomplete dystrophic calcification. This zone of the primary granuloma is hypoxic and is morphol. similar to what has been described for human lung lesions. These results show that this acellular rim may, therefore, be a primary location of persisting bacilli withstanding drug treatment.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TMC207; location of persisting mycobacteria in a guinea pig model of tuberculosis revealed by R207910)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



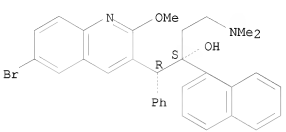
OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (22 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:202669 CA
TITLE: Prospects for non-clinical or clinical development of new antituberculous drugs in relation to corporate strategy
AUTHOR(S): Namba, Kenji
CORPORATE SOURCE: New Product Research Laboratories I, Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: Kekkaku (2006), 81(12), 754-756, 773
CODEN: KEKKAG; ISSN: 0022-9776
PUBLISHER: Nippon Kekkakubyo Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. Tuberculosis (TB) remains one of the deadliest threats to public health. No new anti-TB drugs have been brought into the clinic in the past 40 years. Current non-clin. works with progressed technol. and Global Alliance for TB Drug Development, a non-profit organization established in 2000, accelerate research and development of faster-acting anti-TB compds. We reviewed the status of new types of compds. which are being developed as anti-TB drug, such as diarylquinoline (TMC 207), nitroimidazole (PA-824 & OPC-67683), and moxifloxacin (MFLX). We also

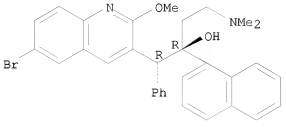
discussed the best clin. development plans for new-TB drugs in relation to corporate strategy.
IT 843663-66-1, TMC 207
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prospects for non-clin. or clin. development of new antituberculous drugs in relation to corporate strategy)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 30 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:157466 CA
TITLE: Diarylquinolines target subunit c of mycobacterial ATP synthase
AUTHOR(S): Koul, Anil; Dendouga, Najoua; Vergauwen, Karen; Molenberghs, Brenda; Vranckx, Luc; Willebrords, Rudy; Ristic, Zorica; Lill, Holger; Dorange, Ismet; Guillemont, Jerome; Bald, Dirk; Andries, Koen
CORPORATE SOURCE: Department of Antimicrobial Research, Tibotec BVBA, Beerse, B-2340, Belg.
SOURCE: Nature Chemical Biology (2007), 3(6), 323-324
CODEN: NCBABT; ISSN: 1552-4450
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The diarylquinoline R207910 (TMC207) is a promising candidate in clin. development for the treatment of tuberculosis. Though R207910-resistant mycobacteria bear mutations in ATP synthase, the compound's precise target is not known. Here we establish by genetic, biochem. and binding assays that the oligomeric subunit c (AtpE) of ATP synthase is the target of R207910. Thus targeting energy metabolism is a new, promising approach for antibacterial drug discovery.
IT 654653-92-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diarylquinolines target subunit c of mycobacterial ATP synthase)
RN 654653-92-6 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αR,βR)-rel- (CA INDEX NAME)

Relative stereochemistry.

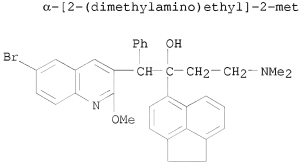


OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 31 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 147:134382 CA
TITLE: Novel quinoline derivative for treating bacterial infection except mycobacteria infection
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

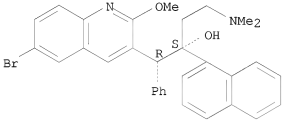
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2006128191	A	20061214	KR 2005-49427	20050609
PRIORITY APPLN. INFO.:			KR 2005-49427	20050609

AB A novel quinoline derivative is provided to be used for treating bacteria infection, except mycobacteria infection.
IT 654654-32-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinoline derivs. for treating bacterial infection)
RN 654654-32-7 CA
CN 3-Quinolineethanol, 6-bromo-α-(1,2-dihydro-5-acenaphthylenyl)-α-[2-(dimethylamino)ethyl]-2-methoxy-β-phenyl- (CA INDEX NAME)



L8 ANSWER 32 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:521297 CA
TITLE: Absolute configuration and structural features of R207910, a novel anti-tuberculosis agent
AUTHOR(S): Petit, S.; Coquerel, G.; Meyer, C.; Guillemont, J.
CORPORATE SOURCE: Sciences et Methodes Separatives, UPRES EA 3233 IRCOF, University of Rouen, Mont Saint Aignan, F-76821, Fr.
SOURCE: Journal of Molecular Structure (2007), 837(1-3), 252-256
CODEN: JMOSB4; ISSN: 0022-2860
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the structure of R207910 ((1R,2S)-1-(6-bromo-2-methoxy-quinolin-3-yl)-4-dimethylamino-2-naphthalen-1-yl-1-phenyl-butan-2-ol, C32H31BrN2O2), the two independent mols. of the asym. unit present similar conformations. They are related to each other by a local pseudo-binary axis whose orientation does not correspond to a defined crystallog. direction of the orthorhombic unit cell, giving rise to an unusual type of supersymmetry. Infinite mol. chains are generated by two types of weak intermol. contacts: Br-Br interactions and π-stacking. The role of these weak contacts and of (CH-π) interactions in the structural cohesion is highlighted, and their possible incidence on supersymmetry is envisaged.
IT 843663-66-1, R207910
RL: PRP (Properties)
(absolute configuration and structural features of novel anti-tuberculosis agent R207910)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:474778 CA
TITLE: A computational model of the inhibition of Mycobacterium tuberculosis ATPase by a new drug candidate R207910
AUTHOR(S): de Jonge, Marc R.; Koymans, Luc H. M.; Guillemont, Jerome E. G.; Koul, Anil; Andries, Koen

CORPORATE SOURCE: MolMo Services BVBA, Turnhout, B2300, Belg.
SOURCE: Proteins: Structure, Function, and Bioinformatics (2007), 67(4), 971-980
CODEN: PSFBAF
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

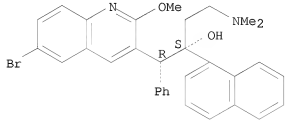
AB Diarylquinolines (DARQs) are a new class of potent inhibitors of the ATPase of Mycobacterium tuberculosis. We have created a homol. model of a binding site for this class of compds. located on the contact area of the a-subunit (gene atpB) and c-subunits (gene atpE) of Mycobacterium tuberculosis ATPase. The binding pocket that was identified from the anal. of the homol. model is formed by 4 helixes of three c-subunits and 2 helixes of the a-subunit. The lead compound of the DARQ series, R207910, was docked into the pocket using a simulated annealing, multiple conformer, docking algorithm. Different stereoisomers were treated sep. The best docking pose for each stereoisomer was optimized by mol. dynamics simulation on the 5300 atoms of the binding region and ligand. The interaction energies in the computed complexes enable us to rank the different stereoisomers in order of interaction strength with the ATPase binding pockets. We propose that the activity of R207910 against Mycobacterium tuberculosis is based on interference of the compound with the escapement geometry of the proton transfer chain. Upon binding the compound mimicks the conserved Arg-186 residue of the a-subunit and interacts in its place with the conserved acidic residue Glu-61 of the c-subunit. This mode of action is corroborated by the good agreement between the computed interaction energies and the observed pattern of stereo-specificity in the model of the binding region.

IT 843663-66-1, R207910
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(computational model of inhibition of Mycobacterium tuberculosis ATPase by a new drug candidate R207910)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

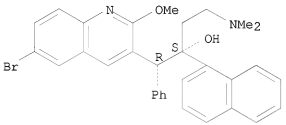


OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 34 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 146:313715 CA
TITLE: New therapeutic strategy for Multi-Drug-Resistant Tuberculosis
AUTHOR(S): Doi, Takao
CORPORATE SOURCE: The Research Institute of Tuberculosis Japan Anti-Tuberculosis Association, Japan
SOURCE: Bunshi Kokyukibyo (2007), 11(1), 109-112
CODEN: BUKOFC; ISSN: 1342-436X
PUBLISHER: Sentan Igakusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review discusses therapeutic application of new drugs including PA-824, Diarylquinoline, moxifloxacin, nitroimidazo-oxazole and new Quinolone in treatment of multi-drug-resistant tuberculosis.
IT 843663-66-1, R 207910
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new therapeutic strategy for multi-drug-resistant tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

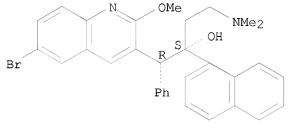
Absolute stereochemistry. Rotation (-).



L8 ANSWER 35 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:291214 CA
TITLE: Multi-drug-resistant Mycobacterium tuberculosis
AUTHOR(S): Tokue, Yutaka
CORPORATE SOURCE: Sch. of Medicine, Gunma Univ., Japan
SOURCE: Lung Perspectives (2005), 13(3), 257-260
CODEN: LUPEFF; ISSN: 0919-5742
PUBLISHER: Medikaru Rebyusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on control of multidrug -resistant M. tubercolosis which is resistant to INH (isoniazid) and RFP (rifampicin), resistance mechanism to antituberculosis, treatment of multidrug resistant M. tuberculosis with e.g. diarylquinoline R207910, advance in diagnosis, etc.
IT 843663-66-1, R207910
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multi-drug-resistant Mycobacterium tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-

α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



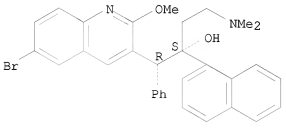
L8 ANSWER 36 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:266208 CA
TITLE: Synergistic activity of R207910 combined with pyrazinamide against murine tuberculosis
AUTHOR(S): Ibrahim, M.; Andries, K.; Lounis, N.; Chauffour, A.; Truffot-Pernot, C.; Jarlier, V.; Veziris, N.
CORPORATE SOURCE: Laboratoire de Bacteriologie, Faculte de Medecine Pitie-Salpetriere, Groupe Hospitalier Pitie-Salpetriere, Assistance Publique Hopitaux de Paris, Universite Pierre et Marie Curie Paris 6 and Centre National de Reference de la Resistance des Mycobacteries aux Antituberculeux, Paris, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(3), 1011-1015
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In previous studies, the diarylquinoline R207910 (also known as TMC207) was demonstrated to have high bactericidal activity when combined with first- or second-line antituberculous drugs. Here we extend the evaluation of R207910 in the curative model of murine tuberculosis by assessing the activities of one-, two-, and three-drug combinations containing R207910 and isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), or moxifloxacin (MXF) in the setting of a high initial bacillary load (7.2 log10 CFU). Two months of treatment with the combinations R207910-PZA, R207910-PZA-INH, R207910-PZA-RIF, or R207910-PZA-MXF resulted in culture-neg. lung homogenates in 70 to 100% of the mice, while mice treated with INH-RIF-PZA (the reference regimen) or RIF-MXF-PZA remained culture pos. Combinations including R207910 but not PZA (e.g., R207910-INH-RIF and R207910-MXF-RIF) were less active than R207910-PZA-containing regimens administered either alone or with the addition of INH, RIF, or MXF. These results reveal a synergistic interaction between R207910 and PZA. Three-drug combinations containing these two drugs and INH, RIF, or MXF have the potential to significantly shorten the treatment duration in patients, provided that these results can be confirmed in long-term expts. including periods of relapse.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(synergistic activity of R207910 combined with pyrazinamide against murine tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 37 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:242883 CA
TITLE: Recent advances in the medical and surgical treatment of multi-drug resistant tuberculosis
AUTHOR(S): Lalloo, Umesh G.; Naidoo, Rishendran; Ambaram, Anish
CORPORATE SOURCE: Division of Respiratory and Critical Care, Department of Medicine, University of KwaZulu-Natal, Durban, S. Afr.
SOURCE: Current Opinion in Pulmonary Medicine (2006), 12(3), 179-185
CODEN: COPMFY; ISSN: 1070-5287
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB Purpose of review: Multi-drug resistant tuberculosis is a serious clin. problem. Extension of drug resistance to second-line anti-tuberculosis drugs in the form of the W-strain is cause for alarm. There is an urgent need for more rapid recognition of multi-drug resistant tuberculosis and newer therapeutic agents. This review summarizes the recent advances in the diagnosis and treatment of multi-drug resistant tuberculosis including surgery and new developments. Recent findings: Multidrug resistant tuberculosis therapy is characterized by prolonged treatment, high morbidity and mortality, and high relapse rates. New diagnostic procedures that include electrophoretic and mol. hybridization techniques will allow rapid diagnosis. Several new drugs are currently in various phases of development. Moxifloxacin, a respiratory fluoroquinolone, is currently in phase III clin. development. New classes of drugs such as nitroimidazopyrans (PA-824) and diarylquinolines (R-207910) are exciting based on phase I and II data. Immunomodulation with vaccines and interferon-γ have been unhelpful. Surgery is reserved for selected cases only. Cure rates of over 90% with reasonable morbidity and

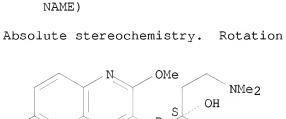
mortality has been achieved with meticulous preoperative preparation, patient selection and careful surgical technique. Summary: Newer drugs and defined indications for surgery should provide improved cure rates, with reduced duration of treatment for multi-drug resistant tuberculosis.

IT 843663-66-1, R-207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new therapeutic agents such as moxifloxacin, nitroimidazopyran PA-824 and diarylquinoline R-207910 may be used for treatment of multi-drug resistant tuberculosis patient)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 38 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 146:229200 CA

TITLE: Preparation of quinoline derivatives as antibacterial agents

INVENTOR(S): Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne; Lancois, David Francis Alain; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Backx, Leo Jacobus Jozef; Meerpoel, Lieven

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014941	A2	20070208	WO 2006-EP64858	20060731
WO 2007014941	A3	20070329		

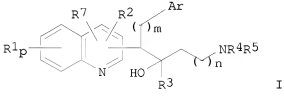
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

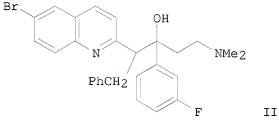
BG 109179	A	20061229	BG 2005-109179		20050609
AU 2006274880	A1	20070208	AU 2006-274880		20060731
CA 2615903	A1	20070208	CA 2006-2615903		20060731
EP 1912648	A2	20080423	EP 2006-778083		20060731
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
JP 2009503025	T	20090129	JP 2008-524509		20060731
US 20080207687	A1	20080828	US 2008-997173		20080129
MX 2008001603	A	20080219	MX 2008-1603		20080201
IN 2008DN00991	A	20080620	IN 2008-DN991		20080205
NO 2008001026	A	20080227	NO 2008-1026		20080227
KR 2008035666	A	20080423	KR 2008-705071		20080229
CN 101277696	A	20081001	CN 2006-80036751		20080402
PRIORITY APPLN. INFO.:			EP 2005-107164	A	20050803
			WO 2006-EP64858	W	20060731

OTHER SOURCE(S): MARPAT 146:229200

GI



I



II

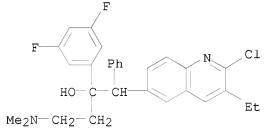
AB Use of a compound for the manufacture of a medicament for the treatment of a bacterial infection provided that the bacterial infection is other than a Mycobacterial infection, said compound being a compound of formula I [Ar = (un)substituted phenyl; R1 = H, halo(alkyl), cyano, etc.; R2 = H, halo, mercapto, etc.; R3 = alkyl, (un)substituted aryl(alkyl) or heterocyclyl(alkyl); R4, R5 = independently H, alkyl or benzyl or R4R5N = heterocyclyl; R7 = H, alkyl, (un)substituted aryl or heterocyclyl; m, n = independently 0-4; p = 1-3], a pharmaceutically acceptable acid or base addition salt, a quaternary amine, a stereochem. isomeric form, a tautomeric form or a N-oxide form thereof. For example, II was provided in a

multi-step synthesis starting from the reaction of 5-bromo-1H-indole-2,3-dione with 4-phenyl-2-butanone. I showed antibacterial activity in Microtitre plate assay.

IT 862543-35-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline derivs. as antibacterial agents)

RN 862543-35-9 CA

CN 6-Quinolineethanol, 2-chloro-α-(3,5-difluorophenyl)-α-[2-(dimethylamino)ethyl]-3-ethyl-β-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 39 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 146:229199 CA

TITLE: Preparation of quinoline derivatives as antibacterial agents

INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne; Lancois, David Francis Alain

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014940	A2	20070208	WO 2006-EP64856	20060731
WO 2007014940	A3	20070329		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006274879	A1	20070208	AU 2006-274879		20060731
CA 2615901	A1	20070208	CA 2006-2615901		20060731
EP 1912647	A2	20080423	EP 2006-778081		20060731
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
JP 2009503024	T	20090129	JP 2008-524508		20060731
IN 2008DN00751	A	20080711	IN 2008-DN751		20080128
US 20080255116	A1	20081016	US 2008-997182		20080129
MX 2008001602	A	20080219	MX 2008-1602		20080201
NO 2008000955	A	20080225	NO 2008-955		20080225
KR 2008038380	A	20080506	KR 2008-705066		20080229
CN 101277695	A	20081001	CN 2006-80036637		20080402
PRIORITY APPLN. INFO.:			EP 2005-107159	A	20050803
			WO 2006-EP64856	W	20060731

OTHER SOURCE(S): MARPAT 146:229199
GI

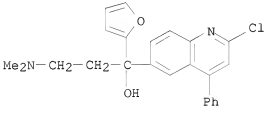
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. represented by the formula I & II [wherein R1 = H, halo(alkyl), aryl, etc.; R2 = H, alkyl(oxy), mercapto, etc.; R3 = alkyl, (un)substituted aryl(alkyl) or heterocyclyl(alkyl); R4, R5 = independently H, alkyl or benzyl, or R4R5N = heterocyclyl; R6 = H or phenyl(alkyl); R7 = H, alkyl, aryl or heterocyclyl; R8 = H or alkyl; R9 = oxo; or R8R9 = -CH=CH-N=; m = 1-3; n = 0-4; and pharmaceutically acceptable acid or base addition salts, quaternary amines, stereoisomers, tautomers or N-oxides thereof] were prepared as antibacterial agents. For example, III was provided in a multi-step synthesis starting from N-(3-bromophenyl)-α-(phenylmethylene)benzeneacetamide. I showed antibacterial activity in Microtitre plate assay.

IT 861872-66-4
RL: PRPH (Prophetic)
(Preparation of quinoline derivatives as antibacterial agents)

RN 861872-66-4 CA

CN 6-Quinolinemethanol, 2-chloro-α-[2-(dimethylamino)ethyl]-α-2-furanyl-4-phenyl- (CA INDEX NAME)



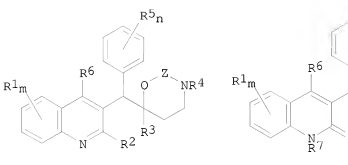
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

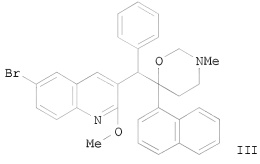
L8 ANSWER 40 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:229198 CA
TITLE: Preparation of quinoline derivatives as antibacterial

agents
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014934	A2	20070208	WO 2006-EP64847	20060731
WO 2007014934	A3	20070405		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006274873	A1	20070208	AU 2006-274873	20060731
CA 2615900	A1	20070208	CA 2006-2615900	20060731
EP 1912649	A2	20080423	EP 2006-792614	20060731
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
JP 2009503021	T	20090129	JP 2008-524502	20060731
IN 2008DN00746	A	20080711	IN 2008-DN746	20080128
US 20080227775	A1	20080918	US 2008-997015	20080128
MX 2008001601	A	20080219	MX 2008-1601	20080201
NO 2008001068	A	20080229	NO 2008-1068	20080229
KR 2008039961	A	20080507	KR 2008-705063	20080229
CN 101277698	A	20081001	CN 2006-80036781	20080402

PRIORITY APPLN. INFO.: EP 2005-107155 A 20050803
WO 2006-EP64847 W 20060731
OTHER SOURCE(S): CASREACT 146:229198; MARPAT 146:229198
GI





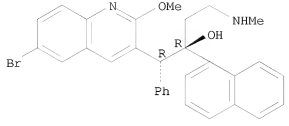
AB Use of a compound for the manufacture of a medicament for the treatment of a bacterial infection provided that the bacterial infection is other than a Mycobacterial infection, said compound being a compound of formula I & II [R1 = H, halo(alkyl), cyano, etc.; R2 = H, halo, mercapto, etc.; R3 = alkyl, (un)substituted aryl(alkyl) or heterocyclyl(alkyl); R4 = H, alkyl or benzyl; R5 = H, halo(alkyl), (aryl)alkyl, etc.; R6 = H, alkyl, (un)substituted aryl or heterocyclyl; R7 = H or alkyl; R8 = oxo; Z = CH2 or C=O; m = 1-4; n = 1-5], a pharmaceutically acceptable acid or base addition salt, a quaternary amine, a stereochem. isomeric form, a tautomeric form or a N-oxide form thereof. For example, III was provided in a multi-step synthesis starting from the reaction of benzenepropanoyl chloride with 4-bromobenzenamine. I showed antibacterial activity in Microtitre plate assay.

IT 654654-75-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline derivs. as antibacterial agents)

RN 654654-75-8 CA

CN 3-Quinolineethanol, 6-bromo-2-methoxy-α-[2-(methylamino)ethyl]-α-1-naphthalenyl-β-phenyl-, (αR,βR)-rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:121847 CA
TITLE: Quinoline derivatives as antibacterial agents and their preparation, pharmaceutical compositions and use in the treatment of bacterial infections
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Guillemont, Jerome Emile Georges; Lancois, David Francis Alain; Motte, Magali Madeleine Simone; Dorange, Ismet; Backx, Leo Jacobus Jozef; Meerpoel, Lieven
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 118pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007000435	A1	20070104	WO 2006-EP63553	20060626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006263883	A1	20070104	AU 2006-263883	20060626
CA 2612619	A1	20070104	CA 2006-2612619	20060626
EP 1898914	A1	20080319	EP 2006-763889	20060626
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008543964	T	20081204	JP 2008-518810	20060626
MX 2008000081	A	20080324	MX 2008-81	20071219
IN 2008DN00349	A	20080815	IN 2008-DN349	20080114

KR 2008021156	A	20080306	KR 2008-702107		20080125
NO 2008000501	A	20080228	NO 2008-501		20080128
CN 101247811	A	20080820	CN 2006-80031055		20080225
PRIORITY APPLN. INFO.:			EP 2005-105762	A	20050628
			WO 2006-EP63553	W	20060626

OTHER SOURCE(S): MARPAT 146:121847
GI

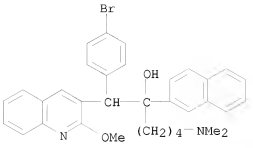
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Use of a compound for the manufacture of a medicament for the treatment of a bacterial infection provided that the bacterial infection is other than a Mycobacterial infection, said compound being a compound of formula I or I a pharmaceutically acceptable acid or base addition salt thereof, a stereochem. isomeric form thereof, a tautomeric form thereof or a N-oxide form thereof, are disclosed. Compds. of formula I and II wherein R1 is H, halo, haloalkyl, CN, OH, (un)substituted aryl, (un)substituted heterocyclyl, (un)substituted alkyl, etc.; p is 1, 2, 3 and 4; R2 is H, OH, mercapto, alkyloxy(alkyloxy), alkylthio, etc.; R3 is (un)substituted alkyl, (un)substituted aryl(alkyl), and (un)substituted heterocyclyl(alkyl); q is 1, 2 and 3; R4 and R5 are independently H, (un)substituted alkyl and benzyl; or R4 and R5 together and including the N to which they are attached may form a ring; R6 is H, halo, haloalkyl, OH, (un)substituted aryl, (un)substituted alkyl, alkyloxy, alkylthio, etc.; r is 1, 2, 3, 4 and 5; R7 is H, (un)substituted alkyl, (un)substituted aryl and (un)substituted heterocyclyl; R8 is H and (un)substituted alkyl; R9 is oxo; or R8 and R9 together form the radical -CH=CH-N=; and their pharmaceutically acid and base addition salts, stereochem. isomeric forms, tautomeric forms, and N-oxides thereof, are claimed. Example compound III was prepared by addition of 3-benzyl-6-bromo-2-methylsulfanylquinoline to 5-(dimethylamino)-1-phenyl-1-pentanone. All the invention compds. were evaluated for their antibacterial activity. Several of the invention compds. showed good activity against several bacteria.

IT 918647-06-0P
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(drug candidate and intermediate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infections)

RN 918647-06-0 CA

CN 3-Quinolineethanol, β-(4-bromophenyl)-α-[4-(dimethylamino)butyl]-2-methoxy-α-2-naphthalenyl- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 42 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:121846 CA
TITLE: Quinoline derivatives as antibacterial agents and their preparation, pharmaceutical compositions and use in the treatment of bacterial infections
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Lancois, David Francis Alain; Motte, Magali Madeleine Simone; Guillemont, Jerome Emile Georges
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 62pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007000434	A1	20070104	WO 2006-EP63552	20060626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006263882	A1	20070104	AU 2006-263882	20060626
CA 2612614	A1	20070104	CA 2006-2612614	20060626
EP 1898909	A1	20080319	EP 2006-763888	20060626
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008546824	T	20081225	JP 2008-518809	20060626
MX 2008000079	A	20080319	MX 2008-79	20071219
IN 2008DN00554	A	20080711	IN 2008-DN554	20080121
NO 2008000499	A	20080229	NO 2008-499	20080128

KR 2008028459	A	20080331	KR 2008-702246		20080128
CN 101252927	A	20080827	CN 2006-80031302		20080227
PRIORITY APPLN. INFO.:			EP 2005-105755	A	20050628
			WO 2006-EP63552	W	20060626

OTHER SOURCE(S): MARPAT 146:121846
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

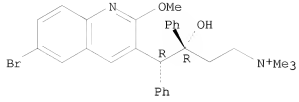
AB Use of a compound for the manufacture of a medicament for the treatment of a bacterial infection provided that the bacterial infection is other than a Mycobacterial infection, said compound being a compound of formula I or II a N-oxide, a tautomeric form or a stereochem. isomeric form thereof. Compds. of formula I and II wherein A- is pharmaceutically acceptable counter ion; R1 is H, halo, haloalkyl, CY, OH, (un)substituted aryl, (un)substituted heterocyclyl, (un)substituted alkyl, etc,; p is 1, 2, 3, and 4; R2 is H, OH, mercapto, alkyloxy(alkyloxy), alkylthio, etc.; R3 is (un)substituted alkyl, (un)substituted aryl(alkyl), and (un)substituted heterocyclyl(alkyl); q is 0, 1, 2, 3, and 4; R4 and R5 are independently H, (un)substituted alkyl, and (un)substituted benzyl; R4R5 together with N may form a heterocyclyl; R6 is H, halo, OH, haloalkyl, (un)substituted aryl, (un)substituted alkyl(oxy), etc.; r is 1, 2, 3, 4, and 5; R7 is H, (un)substituted alkyl, (un)substituted aryl, and (un)substituted heterocyclyl; R8 is H and (un)substituted alkyl; R9 is oxo; R8R9 together may form the radical CH-CH-N=; R10 is (un)substituted alkyl, alkylcarbonyl, (un)substituted aryl(alkyl), etc.; and their N-oxides, tautomers, stereochem. isomeric forms thereof are claimed. The compds. themselves are also claimed as well as their combinations with other antibacterial agents. Example compound III was prepared by methylation of IV with Me iodide. All the invention compds. were evaluated for their antibacterial activity. Several of the tested compds. exhibited good antibacterial activity.

IT 654654-88-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infection)

RN 654654-88-3 CA

CN 3-Quinolinebutanaminium, 6-bromo-γ-hydroxy-2-methoxy-N,N,N-trimethyl-γ,δ-diphenyl-, iodide (1:1), (γR,δR)-rel- (CA INDEX NAME)

Relative stereochemistry.



● I⁻

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 43 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:121844 CA
TITLE: Quinoline derivatives as antibacterial agents and their preparation, pharmaceutical compositions and use in the treatment of bacterial infections
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Guillemont, Jerome Emile Georges; Motte, Magali Madeleine Simone
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 88pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007000436	A1	20070104	WO 2006-EP63556	20060626
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006263884	A1	20070104	AU 2006-263884	20060626
CA 2612623	A1	20070104	CA 2006-2612623	20060626
EP 1898910	A1	20080319	EP 2006-763891	20060626
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JP 2008546825	T	20081225	JP 2008-518812	20060626
MX 2008000082	A	20080324	MX 2008-82	20071219
IN 2008DN00509	A	20080808	IN 2008-DN509	20080118

NO 2008000481	A	20080229	NO 2008-481		20080125
KR 2008028460	A	20080331	KR 2008-702248		20080128
CN 101252928	A	20080827	CN 2006-80031352		20080227
PRIORITY APPLN. INFO.:			EP 2005-105769	A	20050628
			WO 2006-EP63556	W	20060626

OTHER SOURCE(S): MARPAT 146:121844
GI

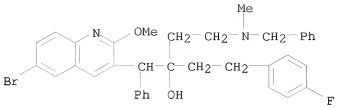
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Use of a compound for the manufacture of a medicament for the treatment of a bacterial infection provided that the bacterial infection is other than a Mycobacterial infection, said compound being a compound of formula I or II a pharmaceutically acceptable acid or base addition salt thereof, a stereochem. isomeric form thereof, a tautomeric form thereof or a N-oxide form thereof. Compds. of formula I and II wherein R1 is H, halo, haloalkyl, CN, OH, (un)substituted aryl, (un)substituted heterocyclyl, (un)substituted alkyl, etc,; p is 1, 2, 3, and 4; R2 is H, OH, mercapto, alkyloxy(alkyloxy), alkylthio, etc.; R3 is (un)substituted aryl and (un)substituted heterocyclyl; R4 and R5 are independently H, (un)substituted alkyl, benzyl; R4R5 together with N may forma a heterocycle; R6 is H, halo, haloalkyl, alkoxy, (un)substituted aryl, (un)substituted alkyl, etc.; r is 1, 2, 3, 4, and 5; R7 is H, (un)substituted alkyl, (un)substituted aryl and (un)substituted heterocyclyl; R8 is H, and (un)substituted alkyl, R9 is oxo; R8R9 together may form the radical CH=CH-N=; A is (un)branched C1-6 alkyl; and their pharmaceutically acceptable acid and base salts, stereochem. isomeric forms, tautomeric forms, and N-oxides thereof, are claimed. Several of these compds. are also claimed as such. Further the combination of the above compds. with other antibacterial agents is described. Example compound III was prepared by addition of 3-benzyl-2-methoxy-6-methylquinoline to 1-(dimethylamino)-5-phenyl-3-pentanone. All the invention compds. were evaluated for their antibacterial activity. From the assay, it was determined that compound III exhibited IC90 values in the range of 1.9 - 37.2 μg/mL against various bacteria.

IT 918518-68-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate and intermediate; preparation of quinoline derivs. as antibacterial agents useful in the treatment of bacterial infections)

RN 918518-68-0 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(4-fluorophenyl)ethyl]-2-methoxy-α-[2-[methyl(phenylmethyl)amino]ethyl]-β-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

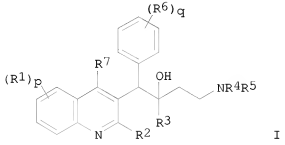
L8 ANSWER 44 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:62607 CA
TITLE: Preparation of aminohydroxyphenylbutylquinolines as antibacterials.
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil; Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne; Lancois, David Francis Alain
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006131519	A1	20061214	WO 2006-EP62934	20060606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2006342109	A	20061221	JP 2005-169982	20050609
CA 2528849	A1	20061208	CA 2005-2528849	20051206
EE 200500034	A	20070215	EE 2005-34	20051206
AU 2005242142	A1	20070104	AU 2005-242142	20051207
MX 2005013412	A	20061207	MX 2005-13412	20051208
US 20060281741	A1	20061214	US 2005-296918	20051208
TR 200504891	A2	20070122	TR 2005-4891	20051208
BR 2005006121	A	20070213	BR 2005-6121	20051208
LV 13534	B	20070620	LV 2005-160	20051209
EP 1901743	A1	20080326	EP 2006-763532	20060606
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

IN 2007DN09841	A	20080118	IN 2007-DN9841		20071219
CN 101232884	A	20080730	CN 2006-80028239		20080201
PRIORITY APPLN. INFO.:			EP 2005-105023	A	20050608
			US 2005-296918	A	20051208
			WO 2006-EP62934	W	20060606

OTHER SOURCE(S): MARPAT 146:626007

GI



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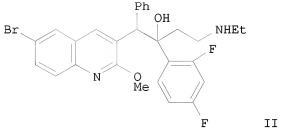


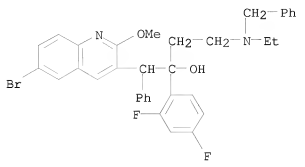
II

AB Use of title compds. [I; R1 = H, halo, polyhaloalkyl, alkyl, hydroxyalkyl, alkoxy, Ar, Het; p, q = 1, 2; R2 = alkoxy, alkoxyalkoxy, alkylthio; R3 = alkyl, Ar, Het, Het1; R4, R5 = H, alkyl, benzyl; R4R5N = (substituted) pyrrolidinyl, pyrrolinyl, pyrrolyl, imidazolidinyl, pyrazolidinyl, imidazolinyl, pyrazolinyl, imidazolyl, pyrazolyl, triazolyl, piperidinyl, pyridinyl, piperazinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, morpholinyl, thiomorpholinyl; R6 = H, halo, polyhaloalkyl, alkyl, alkoxy, alkylthio; 2 vicinal R6 may = CH:CHCH:CH; R7 = H, alkyl, Ar, Het, Het1; Ar = (substituted) Ph, naphthyl, acenaphthyl, 1,2-dihydroacenaphthyl, tetrahydronaphthyl; Het = (substituted) piperidyl, pyrrolyl, N-phenoxypiperidyl, pyrazolyl, triazolyl, imidazolyl, furyl, pyridyl, pyrimidyl, pyrazinyl, etc.; Het1 = (substituted) quinolyl, quinoxalinyl, indolyl, benzimidazolyl, benzofuryl, benzothienyl, 2,3-dihydrobenzodioxinyl, etc.; with provisos], for manufacture of a medicament for treatment of bacterial infection is claimed. Thus, a diastereomer of title compound (II) (preparation outlined) showed an IC90 = 10.8 μg/mL against Streptococcus mutans ATCC33402.

IT 916800-41-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(claimed compound; preparation of aminohydroxyphenylbutylquinolines as antibacterials)

RN 916800-41-4 CA

CN 3-Quinolineethanol, 6-bromo-α-(2,4-difluorophenyl)-α-[2-[ethyl(phenylmethyl)amino]ethyl]-2-methoxy-β-phenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 45 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:45403 CA
TITLE: Process for preparing (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-(1-naphthalenyl)-β-phenyl-3-quinolineethanol
INVENTOR(S): Porstmann, Frank Ralf; Horns, Stefan; Bader, Thomas
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 34pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006125769	A1	20061130	WO 2006-EP62502	20060522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006251208	A1	20061130	AU 2006-251208	20060522
CA 2606675	A1	20061130	CA 2006-2606675	20060522
EP 1888604	A1	20080220	EP 2006-755275	20060522
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

JP 2008545675	T	20081218	JP 2008-512822		20060522
CN 101180302	A	20080514	CN 2006-80017475		20071120
US 20080200683	A1	20080821	US 2007-915204		20071121
MX 2007014874	A	20080215	MX 2007-14874		20071123
KR 2008010453	A	20080130	KR 2007-728419		20071205
IN 2007DN09746	A	20080620	IN 2007-DN9746		20071217
NO 2007006542	A	20071219	NO 2007-6542		20071219
PRIORITY APPLN. INFO.:			EP 2005-104482	A	20050525
			WO 2006-EP62502	W	20060522

OTHER SOURCE(S): CASREACT 146:45403; MARPAT 146:45403

AB The present invention relates to a process for isolating (αS,βR)-6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-(1-naphthalenyl)-β-phenyl-3-quinolineethanol from a mixture of stereoisomeric forms of 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-(1-naphthalenyl)-β-phenyl-3-quinolineethanol (I) by optical resolution with chiral 4-hydroxydinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin 4-oxide or a derivative thereof, in particular (11bR)-4-hydroxydinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin 4-oxide, as resolution agent. I was prepared by reacting 3-(dimethylamino)-1'-propionaphthone with 3-benzyl-6-bromo-2-methoxyquinoline followed by treatment with HOAc/THF.

IT 916329-20-9
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of (±)-quinolineethanol derivative and isolation of (αS,βR)-derivative using chiral dioxaphosphepin 4-oxide)

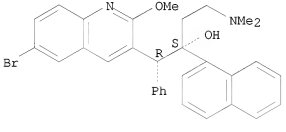
RN 916329-20-9 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)-, compd. with (11bR)-dinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin 4-oxide (1:1) (CA INDEX NAME)

CM 1

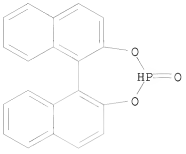
CRN 843663-66-1
CMF C32 H31 Br N2 O2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 681152-46-5
CMF C20 H13 O3 P



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

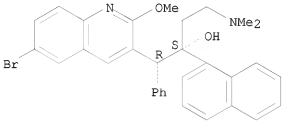
L8 ANSWER 46 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 146:27293 CA
TITLE: Conformational analysis of R207910, a new drug candidate for the treatment of tuberculosis, by a combined NMR and molecular modeling approach
AUTHOR(S): Gaurrand, Sandrine; Desjardins, Stephanie; Meyer, Christophe; Bonnet, Pascal; Argoullon, Jean-Michel; Oulyadi, Hassan; Guillemont, Jerome
CORPORATE SOURCE: Johnson and Johnson Pharmaceutical Research and Development, Val de Reuil, 27106, Fr.
SOURCE: Chemical Biology & Drug Design (2006), 68(2), 77-84 CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB R207910 is an enantiomeric compound from a new class of antimycobacterial agents, the diarylquinolines. As enantiospecific interaction is required for biol. activity, we have undertaken a combined NMR and mol. modeling study to gain new insights into its conformation in solution and its absolute configuration. A conformational anal. using a Monte-Carlo method has been performed on each of the four possible stereomers of this compound leading to the identification of their most stable conformation. Addnl. ab initio calcn. was performed with emphasis on the strength of the observed intramol. hydrogen bond. Simultaneously, a complete structural identification has been carried out by a set of monodimensional and bidimensional 1H-13C-NMR expts. Determination of inter-proton distances has been achieved by a series of 1H-1H ROESY NMR expts. with different mixing times followed by a volume quantification of the correlations peaks. These exptl. data were compared with the theor. distances obtained from the conformational anal. The remarkable match shows that R207910 adopts one of the low-energy conformations predicted by mol. modeling and belongs to the (RS, SR) couple of diastereoisomers. A posteriori validation of our approach has been performed by X-ray structure determination that concluded for the RS configuration.

IT 843663-66-1, R207910
RL: PRP (Properties)
(conformational anal. of R207910, new drug candidate for treatment of

tuberculosis, by combined NMR and mol. modeling approach)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

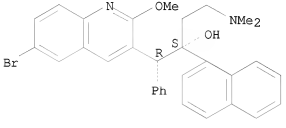


OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:448655 CA
TITLE: Combinations of R207910 with drugs used to treat multidrug-resistant tuberculosis have the potential to shorten treatment duration
AUTHOR(S): Lounis, Nacer; Veziris, Nicolas; Chauffour, Aurelie; Truffot-Pernot, Chantal; Andries, Koen; Jarlier, Vincent
CORPORATE SOURCE: Laboratoire de Bacteriologie, Faculte de Medecine Pitie-Salpetriere, Groupe Hospitalier Pitie-Salpetriere, Universite Pierre et Marie Curie Paris 6, Paris, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(11), 3543-3547
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the present study was to identify the optimal R207910-containing regimen to administer to patients who cannot receive rifampin (RIF) and isoniazid (INH) because of multidrug-resistant tuberculosis (MDR-TB), concomitant use of antiretroviral drugs, or toxicity. Mice were infected i.v. with 5 + 106 CFU of the H37Rv strain and treated five times per wk with R207910 alone or various combinations of R207910 with the second-line drugs amikacin (AMK), pyrazinamide (PZA), moxifloxacin (MXF), and ethionamide (ETH). All R207910-containing regimens were significantly more active than the non-R207910-containing regimens after 1 mo of therapy. When given for 2 mo, R207910 alone was more active than the WHO standard first-line regimen RIF-INH-PZA. When R207910 was combined with second-line drugs, the combinations were more active than the currently recommended regimen of MDR-TB AMK-ETH-MXF-PZA, and culture negativity of both the lungs and spleen was reached after 2 mo of treatment in almost every case.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of R207910 with drugs used to treat multidrug-resistant tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

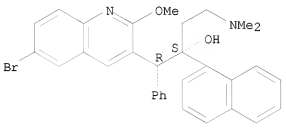


OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 48 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:372598 CA
TITLE: Genetic basis for natural and acquired resistance to the diarylquinoline R207910 in mycobacteria
AUTHOR(S): Petrella, Stephanie; Cambau, Emmanuelle; Chauffour, Aurelie; Andries, Koen; Jarlier, Vincent; Sougakoff, Wladimir
CORPORATE SOURCE: Laboratoire de Recherche Moleculaire sur les Antibiotiques, LRMA INSERM U655, AP-HP CHU Pitie-Salpetriere, Universite Pierre et Marie Curie, Paris, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(8), 2853-2856
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The atpE gene encoding the subunit c of the ATP synthase of Mycobacterium tuberculosis, the target of the new diarylquinoline drug R207910, has been sequenced from in vitro mutants resistant to the drug. The previously reported mutation A63P and a new mutation, I66M, were found. The genetic diversity of atpE in 13 mycobacterial species was also investigated, revealing that the region involved in resistance to R207910 is conserved, except in Mycobacterium xenopi in which the highly conserved residue Ala63 is replaced by Met, a modification that may be associated with the natural resistance of M. xenopi to R207910.
IT 843663-66-1, R207910
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(genetic basis for natural and acquired resistance to diarylquinoline

R207910 in mycobacteria)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 49 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 145:103574 CA
TITLE: Preparation of quinoline derivatives and their use as mycobacterial inhibitors
INVENTOR(S): Koul, Anil; Andries, Koenraad Jozef Lodewijk Marcel
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: Can. Pat. Appl., 62 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2529265	A1	20060624	CA 2005-2529265	20051206
KR 2006073416	A	20060628	KR 2005-49439	20050609
BG 109180	A	20060630	BG 2005-109180	20050609
JP 2006182755	A	20060713	JP 2005-170052	20050609
EE 200500033	A	20060815	EE 2005-33	20051205
AU 2005242138	A1	20060713	AU 2005-242138	20051207
US 20060142279	A1	20060629	US 2005-296992	20051208
WO 2006067048	A1	20060629	WO 2005-EP56594	20051208

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

BR	2005006400	A	20060829	BR 2005-6400		20051208
MX	2005013413	A	20061110	MX 2005-13413		20051208
EP	1830850	A1	20070912	EP 2005-815816		20051208
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
CN	101087608	A	20071212	CN 2005-80044797		20051208
NZ	555460	A	20081128	NZ 2005-555460		20051208
LV	13469	B	20070120	LV 2005-161		20051209
ZA	2007005160	A	20080925	ZA 2007-5160		20070622
IN	2007DN05213	A	20070817	IN 2007-DN5213		20070706
NO	2007003823	A	20070723	NO 2007-3823		20070723
PRIORITY APPLN. INFO.:				EP 2004-78529	A	20041224
				EP 2005-105008	A	20050608
				WO 2005-EP56594	W	20051208

OTHER SOURCE(S): MARPAT 145:103574
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

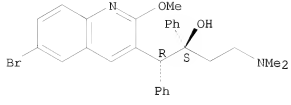
AB The title compds. [I or II; R1 = H, halo, haloalkyl, CN, etc.; p = 0-4; R2 = H, OH, thio, alkoxy, etc.; R3 = alkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl; q = 0-4; R4, R5 = H, alkyl, CH2Ph; or NR4R5 = pyrrolidinyl, imidazolyl, triazolyl, etc.; R6 = H, halo, haloalkyl, etc.; or two vicinal R6 may be taken together to form CH:CHCH:CH; r = 0-5; R7 = H, alkyl, aryl, heteroaryl; R8 = H, alkyl; R9 = oxo; or R8 and R9 together form NCH:CH] which are useful for the treatment of mycobacterial diseases, particularly those diseases caused by pathogenic mycobacteria such as Mycobacterium tuberculosis, M. bovis, M. avium and M. marinum, were prepared In particular, compds. are claimed in which, independently from each other, R1 = Br, p = 1, R2 = alkyloxy, R3 = (un)substituted naphthyl or Ph, q = 1, R4 and R5 each independently = H, Me or Et, R6 = H, r = 0-1 and R7 = H. E.g., a multi-step synthesis of III which showed MIC of 0.34 μg/mL and pIC50 of 8.5 against M. tuberculosis and M. smegmatis, resp., was given. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds. I, the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of mycobacterial diseases and a process for preparing the claimed compds.

IT 654653-59-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinolines as mycobacterial inhibitors)

RN 654653-59-5 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α,β-diphenyl-, (αR,βS)-rel- (CA INDEX NAME)

Relative stereochemistry.



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

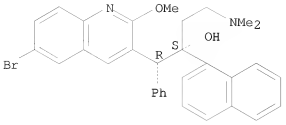
L8 ANSWER 50 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:484498 CA
TITLE: In vitro and in vivo activities of rifampin, streptomycin, amikacin, moxifloxacin, R207910, linezolid, and PA-824 against Mycobacterium ulcerans
AUTHOR(S): Ji, Baohong; Lefrancois, Sebastien; Robert, Jerome; Chauffour, Aurelie; Truffot, Chantal; Jarlier, Vincent
CORPORATE SOURCE: Bacteriologie-Hygiene, Faculte de Medecine Pierre et Marie Curie, Universite Paris 6, Paris, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(6), 1921-1926
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Seven antimicrobials were tested in vitro against 29 clin. isolates of Mycobacterium ulcerans. R207910 demonstrated the lowest MIC50 and MIC90, followed by moxifloxacin (MXF), streptomycin (STR), rifampin (RIF), amikacin (AMK), linezolid (LZD), and PA-824. All but PA-824 demonstrated an MIC90 significantly less than the clin. achievable peak serum level. Administered as monotherapy to mice, RIF, STR, AMK, MXF, R207910, and LZD demonstrated some degree of bactericidal activity, whereas PA-824 failed to prevent mortality and to reduce the mean number of CFU in the footpads. Because 4 or 8 wk of treatment by the combinations RIF-MXF, RIF-R207910, and RIF-LZD displayed bactericidal effects similar to those of RIF-STR and RIF-AMK, 3 combinations might be considered as orally administered combined regimens for treatment of Buruli ulcer. Taking into account the cost, potential toxicity, and availability, the combination RIF-MXF appears more feasible for application in the field; addnl. expts. with mice are warranted to define further its activity against M. ulcerans. In addition, a pilot clin. trial is proposed to test the efficacy of RIF-MXF for treatment of Buruli ulcer.

IT 843663-66-1, R207910
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic susceptibility of Mycobacterium ulcerans and effect of combinations with rifampin)

RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

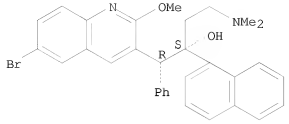
L8 ANSWER 51 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:425198 CA
TITLE: Bactericidal activities of R207910 and other newer antimicrobial agents against Mycobacterium leprae in mice
AUTHOR(S): Ji, Baohong; Chauffour, Aurelie; Andries, Koen; Jarlier, Vincent
CORPORATE SOURCE: Bacteriologie-Hygiene, Faculte de Medecine Pierre et Marie Curie, Universite Paris 6, Paris, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(4), 1558-1560
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As measured by a proportional bactericidal technique in the mouse footpad system, the bactericidal activity against Mycobacterium leprae of R207910 was equal to that of rifapentine, rifampin, or moxifloxacin and significantly greater than those of minocycline, PA-824, and linezolid. These data suggest that R207910 may play an important role in treatment of leprosy.

IT 843663-66-1, R207910
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bactericidal activities of R207910 and other newer antimicrobial agents against Mycobacterium leprae in mice)

RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 52 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 144:365369 CA
TITLE: Crystal structure of ATP synthase atpE subunit of drug-resistant and drug-sensitive microbacterial strains, and drug screening applications
INVENTOR(S): Andries, Koenraad Jozef Lodewijk Marcel; Goehlmann, Hinrich Wilhelm Helmut; Neefs, Jean-Marc Edmond Fernand Marie; Verhasselt, Peter Karel Maria; Winkler, Johann; De Jonge, Marc Rene; Koymans, Lucien Maria Henricus
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006035051	A1	20060406	WO 2005-EP54893	20050928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005288848	A1	20060406	AU 2005-288848	20050928
CA 2579971	A1	20060406	CA 2005-2579971	20050928
EP 1797115	A1	20070620	EP 2005-794520	20050928
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101065397	A	20071031	CN 2005-80040762	20050928

JP 2008515395	T	20080515	JP 2007-532910		20050928
IN 2007DN02272	A	20070803	IN 2007-DN2272		20070323
ZA 2007002540	A	20080827	ZA 2007-2540		20070327
NO 2007002237	A	20070625	NO 2007-2237		20070430
PRIORITY APPLN. INFO.:			EP 2004-104720	A	20040928
			US 2004-620500P	P	20041020
			WO 2005-EP54893	W	20050928

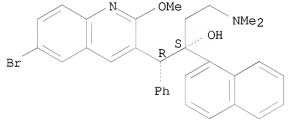
AB The present invention provides the crystal structure and the atomic structure coordinates of the atpE protein which is the C chain of the F0 subunit of F0F1-ATPase complex (ATP synthase) of DARQ J (R207910)-sensitive and DARQ J-resistant strains of Mycobacterium tuberculosis and M. smegmatis. This invention provides an isolated mutant atpE protein and departing from said mutant atpE protein the identification of an ATPase binding domain. This invention also provides related nucleic acids, vectors, host cells, pharmaceutical compns. and articles of manufacture This invention further provides methods for determining whether a test compound interacts with an atpE protein, i.e. with the ATPase binding domain of the present invention, as well as pharmaceuticals compns. comprising said test compound, in particular as antimicrobials, more particular as antimycobacterial agent, even more particular for treating tuberculosis in a subject.

IT 843663-66-1, R207910
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal structure of ATP synthase atpE subunit of drug-resistant and drug-sensitive microbacterial strains, and drug screening applications)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT:	1	THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 53 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	144:51462 CA
TITLE:	Preparation of aminohydroxyaralkylquinolines for the treatment of drug resistant mycobacterial diseases
INVENTOR(S):	Andries, Koenraad Jozef Lodewijk Marcel; Van Gestel, Jozef Frans Elisabetha
PATENT ASSIGNEE(S):	Janssen Pharmaceutica N.V., Belg.
SOURCE:	PCT Int. Appl., 56 pp. CODEN: PIXXD2

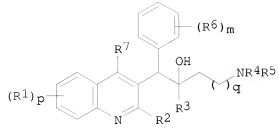
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005117875	A1	20051215	WO 2005-EP52371	20050524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005249231	A1	20051215	AU 2005-249231	20050524
CA 2566544	A1	20051215	CA 2005-2566544	20050524
EP 1753427	A1	20070221	EP 2005-743054	20050524
EP 1753427	B1	20080402		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1976704	A	20070606	CN 2005-80017016	20050524
BR 2005010414	A	20071023	BR 2005-10414	20050524
JP 2008500992	T	20080117	JP 2007-513922	20050524
AT 390925	T	20080415	AT 2005-743054	20050524
ES 2306146	T3	20081101	ES 2005-743054	20050524
IN 2006DN06315	A	20070831	IN 2006-DN6315	20061027
MX 2006013888	A	20070126	MX 2006-13888	20061128
KR 2007017393	A	20070209	KR 2006-724974	20061128
US 20070249667	A1	20071025	US 2006-569681	20061128
NO 2006006041	A	20070227	NO 2006-6041	20061228

PRIORITY APPLN. INFO.:

EP 2004-102402	A	20040528	
EP 2005-743054	A	20050524	
WO 2005-EP52371	W	20050524	

OTHER SOURCE(S): MARPAT 144:51462
GI



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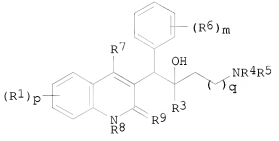


II

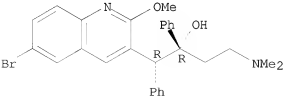
AB Use of title compds. [I, II; R1 = H, halo, haloalkyl, cyano, OH, aryl, heterocyclyl, alkyl, alkoxy, alkylthio, alkoxyalkyl, etc.; p = 1-4; R2 = H, OH, SH, alkoxy, alkylthio, alkylamino, etc.; R3 = alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkyl; q = 0-4; R4, R5 = H, alkyl, PhCH2; R4R5N = (substituted) pyrrolidinyl, imidazolyl, morpholinyl, thiomorpholinyl, pyrazinyl, etc.; R6 = H, halo, haloalkyl, OH, aryl, alkyl, alkoxy, alkylthio, aralkyl, etc.; 2 vicinal R6 = CH:CHCH:CH; m = 1-5; R7 = H, alkyl, aryl, heterocyclyl; R8 = H, alkyl; R9 = O; R8R9 = NCH:CH] for preparation of a medicament for treatment of an infection with a drug resistant Mycobacterium strain is claimed. Title compds. showed min. inhibitory concns. of 0.06-0.12 mg/L against isoniazid-resistant M. tuberculosis.

IT 654653-58-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminohydroxyaralkylquinolines for the treatment of drug resistant mycobacterial diseases)

RN 654653-58-4 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α,β-diphenyl-, (αR,βR)-rel- (CA INDEX NAME)

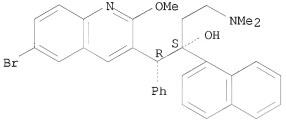
Relative stereochemistry.



OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 54 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:325675 CA
TITLE: Research advances: New weapon in war on TB
AUTHOR(S): King, Angela G.
CORPORATE SOURCE: Wake Forest University, Winston-Salem, NC, 27109, USA
SOURCE: Journal of Chemical Education (2005), 82(8), 1114-1115
CODEN: JCEDA8; ISSN: 0021-9584
PUBLISHER: Journal of Chemical Education, Dept. of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The concerted efforts of the researchers from Johnson & Johnson Pharmaceutical Research and Development, the Swedish Institute for Infections Disease Control and The Pitie-Salpetriere School of Medicine revealed a new anti-tuberculosis (TB) compound by testing prototypes of different chemical series in a whole cell assay against Mycobacterium smegmatis. The R207910 has a potent early bactericidal activity in the nonestablished infection murine TB model. It attacks a different target from existing anti-TB drugs, inhibiting ATP synthase. Shutting down ATP synthase may result in ATP depletion and imbalance in pH homeostasis. Both of these factors lead to decreased survival for the target microorganism. The specificity of R207910 against mycobacteria is due to differences in ATP synthase sequences in eukaryotes and bacteria.
IT 843663-66-1, R 207910
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of anti-TB compound)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 55 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:259311 CA
TITLE: New drugs being developed for the treatment of tuberculosis
AUTHOR(S): Doggrell, Sheila A.

CORPORATE SOURCE: School of Nursing, Auckland University of Technology-Akoranga Campus, Auckland, N. Z.
SOURCE: Expert Opinion on Investigational Drugs (2005), 14(7), 917-920
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

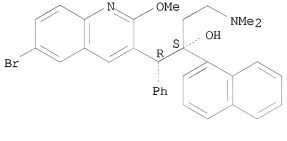
AB A review. More than one-third of the world is infected with tuberculosis (TB) and 5000 people die of TB everyday. Of the many diarylquinolones shown to be effective at inhibiting the multiple-cycle growth of Mycobacterium tuberculosis, R-207910 was the most active and was chosen as the lead compound In the nonestablished infection mouse TB model, a single dose of R-207910 50 mg/kg had a bacteriostatic effect, and a bactericidal effect was observed at 100 mg/kg. In the established infection mouse model, treatment was started 12-14 days after infection, and when added to the triple therapy of isoniazid, rifampin, and pyrazinamide or substituted for any component of the triple therapy, R-207910 increased the effectiveness. As ethambutol is chemical simple, and only has modest potency in treating TB, it was considered to be amenable to optimization by combinatorial chemical, and from the analogs synthesized that inhibited the growth of M. tuberculosis, SQ-109 was eventually selected as the lead compound for further testing. In female mice infected with M. tuberculosis H37Rv by tail-vein injection, treatment with SQ-109 25 mg orally initiated 20 days later for 5 days/wk for 4 wk reduced the counts by 1.87 log units, which was slightly more than with ethambutol 100 mg (1.67 log units). These results indicate that exciting new drugs are under development for the treatment of TB.

IT 843663-66-1, R 207910
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new drugs being developed for treatment of tuberculosis)

RN 843663-66-1 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 56 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:229731 CA

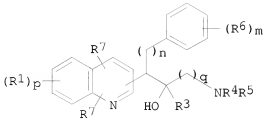
TITLE: Preparation of aminohydroxyalkylquinolines as mycobacterial inhibitors
INVENTOR(S): Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne; Lancois, David Francis Alain
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075428	A1	20050818	WO 2005-EP50375	20050128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005210036	A1	20050818	AU 2005-210036	20050128
CA 2554049	A1	20050818	CA 2005-2554049	20050128
EP 1713776	A1	20061025	EP 2005-707886	20050128
EP 1713776	B1	20080514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1910154	A	20070207	CN 2005-80003129	20050128
BR 2005007312	A	20070626	BR 2005-7312	20050128
JP 2007519687	T	20070719	JP 2006-550188	20050128
AT 395336	T	20080515	AT 2005-707886	20050128
ES 2306098	T3	20081101	ES 2005-707886	20050128
NZ 547614	A	20090430	NZ 2005-547614	20050128
US 20070299106	A1	20071227	US 2006-422152	20060605
KR 2007004597	A	20070109	KR 2006-715159	20060727
IN 2006DN04331	A	20070713	IN 2006-DN4331	20060727
MX 2006008596	A	20060828	MX 2006-8596	20060728
ZA 2006006291	A	20080227	ZA 2006-6291	20060728
NO 2006003821	A	20060828	NO 2006-3821	20060828

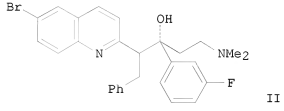
PRIORITY APPLN. INFO.:

EP 2004-75286	A	20040129
EP 2005-707886	A	20050128
WO 2005-EP50375	W	20050128

OTHER SOURCE(S): CASREACT 143:229731; MARPAT 143:229731
GI



I



II

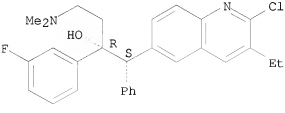
AB Title compds. [I; R1 = H, halo, haloalkyl, cyano, OH, Ar, Het, alkyl, alkoxy, alkylthio, alkoxyalkyl, etc.; p = 1-3; n, q = 0-4; R2 = H, halo, alkyl, OH, SH, (substituted) alkoxy, etc.; R3 = alkyl, Ar, Het, etc.; R4, R5 = H, alkyl, PhCH2; R4R5N = pyrrolidinyl, pyrrolyl, pyrrolinyl, imidazolidinyl, pyrazolidinyl, etc.; R6 = H, halo, haloalkyl, OH, Ar, alkyl, alkoxy, alkylthio, alkoxyalkyl, alkylthioalkyl, etc.; 2 vicinal R6 = atoms to form a fused benzene ring; R7 = H, alkyl, Ar, Het; Ar = (substituted) Ph, naphthyl, acenaphthyl, tetrahydronaphthyl; Het = (substituted) N-phenoxypiperidinyl, pyrrolyl, pyrazolyl, imidazolyl, furyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolinyl, indolyl, indazolyl, benzofuryl, benzothienyl, etc.], were prepared Thus, title compound (II) (preparation given) showed a pIC50 = 6.5 against M. smegmatis.

IT 862543-33-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminohydroxyalkylquinolines as mycobacterial inhibitors)

RN 862543-33-7 CA

CN 6-Quinolineethanol, 2-chloro-α-[2-(dimethylamino)ethyl]-3-ethyl-α-(3-fluorophenyl)-β-phenyl-, (αR,βS)-rel- (CA INDEX NAME)

Relative stereochemistry.



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 57 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:194012 CA
TITLE: Preparation of oxazinylbenzylquinolines as mycobacterial inhibitors.
INVENTOR(S): Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070924	A1	20050804	WO 2005-EP50267	20050121
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005206330	A1	20050804	AU 2005-206330	20050121
CA 2553266	A1	20050804	CA 2005-2553266	20050121
EP 1711492	A1	20061018	EP 2005-701586	20050121
EP 1711492	B1	20080416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1910177	A	20070207	CN 2005-80002679	20050121
BR 2005007076	A	20070619	BR 2005-7076	20050121
JP 2007518775	T	20070712	JP 2006-550174	20050121
AT 392423	T	20080515	AT 2005-701586	20050121
ES 2306082	T3	20081101	ES 2005-701586	20050121
US 20070082895	A1	20070412	US 2006-596386	20060612
US 7338949	B2	20080304		
KR 2006127016	A	20061211	KR 2006-713237	20060630
MX 2006008313	A	20060929	MX 2006-8313	20060721
IN 2006DN04215	A	20070629	IN 2006-DN4215	20060721
ZA 2006006070	A	20071227	ZA 2006-6070	20060721
NO 2006003747	A	20060822	NO 2006-3747	20060822

PRIORITY APPLN. INFO.: US 2004-538768P P 20040123
WO 2005-EP50267 W 20050121
OTHER SOURCE(S): CASREACT 143:194012; MARPAT 143:194012
GI

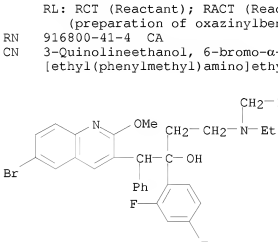
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I, II; R1 = H, halo, haloalkyl, cyano, OH, Ar, Het, alkyl, alkoxy, alkylthio, alkyloxyalkyl, alkylthioalkyl, aralkyl, diarylalkyl; p = 1-4; R2 = H, OH, SH, alkoxy, alkoxyalkoxy, alkylthio, mono or dialkylamino, piperidinyl, morpholino, thiomorpholino, (alkyl)piperazinyl; R3 = alkyl, Ar, aralkyl, Het, Het-alkyl; R4 = H, alkyl, benzyl; R5 = H, halo, haloalkyl, OH, Ar, alkyl, alkoxy, alkylthio, alkoxyalkyl, alkylthioalkyl, Aralkyl, diarylalkyl; 2 vicinal R5 = atoms to form a fused Ph ring; n = 1-5; R6 = H, alkyl, Ar, Het; R7 = H, alkyl; R8 = O; or R7R8 = CH:CHN:; Z = CH2, CO; Ar = (substituted) Ph, naphthyl, acenaphthyl, tetrahydronaphthyl; Het = (substituted) N-phenoxypiperidinyl, pyrrolyl, pyrazolyl, imidazolyl, furyl, thienyl, oxazolyl, isoxazolyl, benzothiazolyl, benzothienyl, etc.], were prepared Thus, title compound (III) (prepared via cyclocondensation of paraformaldehyde with the corresponding aminoalc.) showed pIC50 = 8.5 against M. smegmatis ATCC607.

IT 916800-41-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of oxazinylbenzylquinolines as mycobacterial inhibitors)

RN 916800-41-4 CA

CN 3-Quinolineethanol, 6-bromo-α-(2,4-difluorophenyl)-α-[2-[ethyl(phenylmethyl)amino]ethyl]-2-methoxy-β-phenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 58 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:193916 CA

TITLE: Preparation of (aminohydroxyalkyl)quinolines as mycobacterial inhibitors

INVENTOR(S): Guillemont, Jerome Emile Georges; Pasquier, Elisabeth Therese Jeanne; Lancois, David Francis Alain

PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.

SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070430	A1	20050804	WO 2005-EP50271	20050121
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005205935	A1	20050804	AU 2005-205935	20050121
CA 2553269	A1	20050804	CA 2005-2553269	20050121
EP 1711181	A1	20061018	EP 2005-701589	20050121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1909907	A	20070207	CN 2005-80002654	20050121
BR 2005007065	A	20070612	BR 2005-7065	20050121
JP 2007518776	T	20070712	JP 2006-550175	20050121
US 20070093478	A1	20070426	US 2006-596270	20060607
KR 2007001929	A	20070104	KR 2006-714657	20060720
MX 2006008315	A	20060929	MX 2006-8315	20060721
IN 2006DN04218	A	20070713	IN 2006-DN4218	20060721
ZA 2006006066	A	20071128	ZA 2006-6066	20060721
NO 2006003748	A	20060822	NO 2006-3748	20060822
PRIORITY APPLN. INFO.:			US 2004-538907P P	20040123
			WO 2005-EP50271 W	20050121
OTHER SOURCE(S):	CASREACT 143:193916; MARPAT 143:193916			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

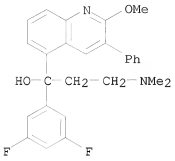
AB Title compds. [I, II; R1 = H, halo, haloalkyl, cyano, OH, Ar, Het, etc.; p = 1-3; R2 = H, alkyl, OH, SH, (substituted) alkoxy, etc.; R3 = alkyl Ar, Het, etc.; q = 0-4; X = bond, CH2; R4, R5 = H, alkyl, PhCH2; R4R5N = (substituted) pyrrolidinyl, imidazolyl, thiomorpholinyl, piperazinyl, pyrrolyl, pyrazolidinyl, pyridinyl, etc.; R6 = H, (substituted) phenyl(alkyl); R7 = H, alkyl, Ar, Het; R8 = H, alkyl; R9 = O; R8R9 = CH:CHN:; Ar = (substituted) Ph, naphthyl, acenaphthyl, tetrahydronaphthyl; Het = (substituted) N-phenoxypiperidinyl, pyrrolyl, pyrazolyl, imidazolyl, furyl, pyrimidinyl, indolyl, indazolyl, benzimidazolyl, etc.], were prepared Thus, title compound (III) showed pIC50 = 6.6 against M. smegmatis ATCC607.

IT 861871-52-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminohydroxyalkyl)quinolines as mycobacterial inhibitors)

RN 861871-52-5 CA

CN 5-Quinolinemethanol, α-(3,5-difluorophenyl)-α-[2-

(dimethylamino)ethyl]-2-methoxy-3-phenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 59 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:97278 CA
TITLE: Preparation of quinoline derivatives and their use as mycobacterial inhibitors
INVENTOR(S): Van Gestel, Jozef Frans Elisabetha; Guillemont, Jerome Emile Georges; Venet, Marc Gaston; Poignet, Herve Jean Joseph; Decrane, Laurence Francoise Bernadette; Vernier, Daniel F. J.; Odds, Frank Christopher
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: U.S. Pat. Appl. Publ., 31 pp., Cont.-in-part of Appl. No. PCT/EP03/50322.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050148581	A1	20050707	US 2004-7026	20041208
US 7498343	B2	20090303		
WO 2004011436	A1	20040205	WO 2003-EP50322	20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 101070304	A	20071114	CN 2007-10104947	20030718

PRIORITY APPLN. INFO.:
US 2002-398711P P 20020725
WO 2003-EP50322 A2 20030718
CN 2003-817713 A3 20030718

OTHER SOURCE(S): MARPAT 143:97278

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

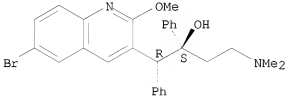
AB The title compds. [I or II; R1 = H, halo, haloalkyl, CN, etc.; p = 0-4; R2 = H, OH, thio, alkoxy, etc.; R3 = alkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl; q = 0-4; R4, R5 = H, alkyl, CH2Ph; or NR4R5 = pyrrolidinyl, imidazolyl, triazolyl, etc.; R6 = H, halo, haloalkyl, etc.; or two vicinal R6 may be taken together to form CH:CHCH:CH; r = 0-5; R7 = H, alkyl, aryl, heteroaryl; R8 = H, alkyl; R9 = oxo; or R8 and R9 together form NCH:CH] which are useful for the treatment of mycobacterial diseases, particularly those diseases caused by pathogenic mycobacteria such as Mycobacterium tuberculosis, M. bovis, M. avium and M. marinum, were prepared In particular, compds. are claimed in which, independently from each other, R1 = Br, p = 1, R2 = alkyloxy, R3 = (un)substituted naphthyl or Ph, q = 1, R4 and R5 each independently = H, Me or Et, R6 = H, r = 0-1 and R7 = H. E.g., a multi-step synthesis of III which showed MIC of 0.34 μg/mL and pIC50 of 8.5 against M. tuberculosis and M. smegmatis, resp., was given. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds. I, the use of the claimed compds. or compns. for the manufacture of a medicament for the treatment of mycobacterial diseases and a process for preparing the claimed compds.

IT 654653-59-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinolines as mycobacterial inhibitors)

RN 654653-59-5 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α,β-diphenyl-, (αR,βS)-rel- (CA INDEX NAME)

Relative stereochemistry.



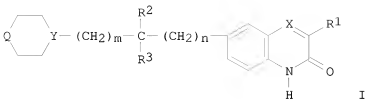
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 60 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:78213 CA
TITLE: Preparation of cyclohexylalkyl quinolinone and quinoxalinone derivatives as poly(ADP-ribose) polymerase (PARP) inhibitors
INVENTOR(S): Mabire, Dominique Jean-Pierre; Van Dun, Jacobus Alphonsus Josephus; Somers, Maria Victorina Francisca; Wouters, Walter Boudewijn Leopold

PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058843	A1	20050630	WO 2004-EP13165	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004299183	A1	20050630	AU 2004-299183	20041118
CA 2548273	A1	20050630	CA 2004-2548273	20041118
EP 1694653	A1	20060830	EP 2004-803192	20041118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
CN 1890225	A	20070103	CN 2004-80036656	20041118
BR 2004017571	A	20070320	BR 2004-17571	20041118
JP 2007513898	T	20070531	JP 2006-543409	20041118
SG 151250	A1	20090430	SG 2009-1548	20041118
US 20090042881	A1	20090212	US 2006-596083	20060530
MX 2006006573	A	20060731	MX 2006-6573	20060609
IN 2006DN03331	A	20070824	IN 2006-DN3331	20060609
ZA 2006004774	A	20071128	ZA 2006-4774	20060609
KR 2006108753	A	20061018	KR 2006-713344	20060703
NO 2006003129	A	20060705	NO 2006-3129	20060705
PRIORITY APPLN. INFO.:			EP 2003-78918 A	20031210
			WO 2004-EP13165 W	20041118

OTHER SOURCE(S): CASREACT 143:78213; MARPAT 143:78213
GI



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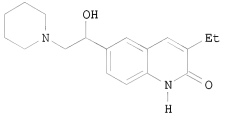


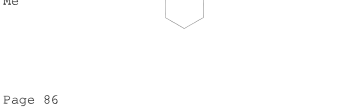
II

AB Title compds. I [n = 0-1; m = 0-1; X = N, CR4; Y = N, CH; Q = NH, O, CO, etc.; R1 = alkyl, thienyl; R2 = H or together with R3 may form O; R3 = H, alkyl, OH, etc. or R3 = (CH2)pZ; R4 = H or together with R1 may form (CH=CH)2; p = 0-2; Z = (un)substituted heterocycle] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of poly(ADP-ribose) polymerase (PARP). Thus, e.g., II was prepared by reaction of 3-ethyl-2(1H)-quinolinone with chloro-acetyl chloride followed by coupling with piperidine and subsequent reduction The inhibitory activity of I towards PARP-1 was evaluated in scintillation proximity assays and in filtration assays and it was revealed that compds. of the invention displayed inhibitory activity at initial test concns. of 10-6 and 10-5 M, resp. I as inhibitors of poly(ADP-ribose) polymerase should prove useful in the treatment of PARP-1 mediated disorders. Pharmaceutical compns. comprising I are disclosed.

IT 855444-77-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclohexylalkyl quinolinone and quinoxalinone derivs. as poly(ADP-ribose) polymerase (PARP) inhibitors)

RN 855444-77-8 CA

CN 6-Quinolinemethanol, α-cyclohexyl-3-ethyl-2-methoxy-α-[2-(4-methyl-1-piperazinyl)ethyl]- (CA INDEX NAME)



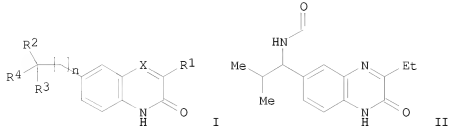
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 61 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 143:60003 CA
TITLE: Preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors
INVENTOR(S): Mabire, Dominique Jean-Pierre; Guillemont, Jerome Emile Georges; Van Dun, Jacobus Alphonsus Josephus; Somers, Maria Victorina Francisca; Wouters, Walter Boudewijn Leopold
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054210	A1	20050616	WO 2004-EP13164	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004295059	A1	20050616	AU 2004-295059	20041118
CA 2546657	A1	20050616	CA 2004-2546657	20041118
EP 1709012	A1	20061011	EP 2004-819602	20041118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
CN 1890224	A	20070103	CN 2004-80035857	20041118
BR 2004016532	A	20070109	BR 2004-16532	20041118
JP 2007513101	T	20070524	JP 2006-541830	20041118
SG 151249	A1	20090430	SG 2009-1531	20041118
IN 2006DN03071	A	20070810	IN 2006-DN3071	20060529
US 20070129375	A1	20070607	US 2006-596086	20060530
MX 2006006255	A	20060809	MX 2006-6255	20060602
KR 2006118534	A	20061123	KR 2006-711234	20060608
NO 2006003028	A	20060628	NO 2006-3028	20060628

PRIORITY APPLN. INFO.: EP 2003-78859 A 20031205
WO 2004-EP13164 W 20041118

OTHER SOURCE(S): CASREACT 143:60003; MARPAT 143:60003
GI



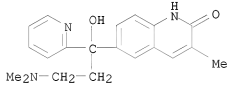
I II

AB The title compds. I [n = 0-2; X = N, CR5; R5 = H or taken together with R1 may form CH:CHCH:CH; R1 = alkyl, thienyl; R2 = H, OH, or taken together with R3 or R4 may form O; R3 = OH, OR8, SR9, etc.; R8 = alkyl, alkylcarbonyl, dialkylaminoalkyl; R9 = dialkylaminoalkyl; R4 = H, alkyl, furanyl, etc.; with the provision], useful for the treatment of a PARP mediated disorder, were prepared E.g., a multi-step synthesis of II, starting from 1-(4-amino-3-nitrophenyl)-2-methyl-1-propanone, was given. The exemplified compds. I were tested in an in vitro assay based on SPA technol. and in an in vitro filtration assay assessing PARP-1 activity (data given). The pharmaceutical composition comprising the compound I is disclosed.

IT 854523-92-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

RN 854523-92-5 CA

CN 2(1H)-Quinolinone, 6-[3-(dimethylamino)-1-hydroxy-1-(2-pyridinyl)propyl]-3-methyl- (CA INDEX NAME)



$Me_2N-CH_2-CH_2$

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 62 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:60002 CA

TITLE: Preparation of 7-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors

INVENTOR(S): Mabire, Dominique Jean-pierre; Guillemont, Jerome Emile Georges; Van Dun, Jacobus Alphonsus Josephus; Somers, Maria Victorina Francisca; Wouters, Walter Boudewijn Leopold

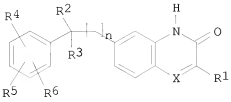
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005054209	A1	20050616	WO 2004-EP13162		20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004295057	A1	20050616	AU 2004-295057		20041118
CA 2546002	A1	20050616	CA 2004-2546002		20041118
EP 1709011	A1	20061011	EP 2004-819600		20041118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU					
CN 1882549	A	20061220	CN 2004-80034287		20041118
BR 2004016817	A	20070306	BR 2004-16817		20041118
JP 2007513087	T	20070524	JP 2006-540337		20041118
SG 150534	A1	20090330	SG 2009-1198		20041118
US 20080249099	A1	20081009	US 2006-595882		20060517
IN 2006DN02810	A	20070803	IN 2006-DN2810		20060518
MX 2006005686	A	20060817	MX 2006-5686		20060519
ZA 2006004076	A	20070926	ZA 2006-4076		20060519
KR 2006111532	A	20061027	KR 2006-710200		20060525
NO 2006002892	A	20060809	NO 2006-2892		20060620
PRIORITY APPLN. INFO.:			EP 2003-78650	A	20031120
			WO 2004-EP13162	W	20041118

OTHER SOURCE(S): CASREACT 143:60002; MARPAT 143:60002
GI



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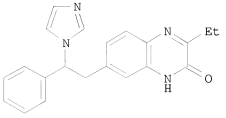


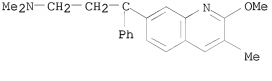
II

AB The title compds. I [n = 0-2; X = N, CR7; R7 = H or taken together with R1 may form CH:CHCH:CH; R1 = alkyl, thienyl; R2 = H, OH, alkyl, alkynyl or taken together with R3 may form O; R3 = OH, OR10, SR11, etc.; R10 = alkyl, alkylcarbonyl, dialkylaminoalkyl; R11 = dialkylaminoalkyl; R4-R6 = H, halo, trihalomethyl, etc.; with the provision], useful for the treatment of a PARP mediated disorder, were prepared E.g., a multi-step synthesis of II, starting from N-[4-(2-oxo-2-phenylethyl)phenyl]acetamide, was given. The exemplified compds. I were tested in an in vitro assay based on SPA technol. and in an in vitro filtration assay assessing PARP-1 activity (data given). The pharmaceutical composition comprising the compound I is disclosed.

IT 854398-84-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 7-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

RN 854398-84-8 CA

CN 7-Quinolinemethanol, α-[2-(dimethylamino)ethyl]-2-methoxy-3-methyl-α-phenyl- (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

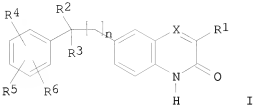
L8 ANSWER 63 OF 67 CA COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 143:60001 CA
TITLE: Preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors
INVENTOR(S): Mabire, Dominique Jean-pierre; Guillemont, Jerome Emile Georges; Van Dun, Jacobus Alphonsus Josephus; Somers, Maria Victorina Francisca; Wouters, Walter Boudewijn Leopold
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054201	A1	20050616	WO 2004-EP13163	20041118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004295058	A1	20050616	AU 2004-295058	20041118
CA 2546300	A1	20050616	CA 2004-2546300	20041118
EP 1687277	A1	20060809	EP 2004-819601	20041118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1882547	A	20061220	CN 2004-80034176	20041118
BR 2004016206	A	20061226	BR 2004-16206	20041118
JP 2007511574	T	20070510	JP 2006-540338	20041118
SG 150533	A1	20090330	SG 2009-1197	20041118
US 20070072842	A1	20070329	US 2006-595891	20060518
IN 2006DN02813	A	20070803	IN 2006-DN2813	20060518
MX 2006005687	A	20060817	MX 2006-5687	20060519
ZA 2006004075	A	20070926	ZA 2006-4075	20060519
KR 2006115393	A	20061108	KR 2006-710201	20060525
NO 2006002894	A	20060809	NO 2006-2894	20060620

PRIORITY APPLN. INFO.:			
	WO 2003-EP13028	A	20031120
	EP 2003-78860	A	20031205
	WO 2003-EP130	A	20031120
	WO 2004-EP13163	W	20041118

OTHER SOURCE(S): CASREACT 143:60001; MARPAT 143:60001
GI



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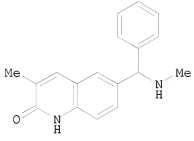


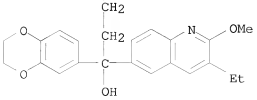
II

AB The title compds. I [n = 0-2; X = N, CR7; R7 = H or taken together with R1 may form CH:CHCH:CH; R1 = alkyl, thiophenyl; R2 = H, OH, alkyl, alkynyl or taken together with R3 may form O; R3 = OH, OR10, SR11, etc.; R10, R11 = CHO, alkyl, (alkyl)amino, etc.; R4-R6 = H, halo, trihalomethyl, etc.; with the provision], useful for the treatment of a PARP mediated disorder, were prepared E.g., a multi-step synthesis of II, starting from bromobenzene and 3-methyl-6-quinolinecarboxaldehyde, was given. The exemplified compds. I were tested in an in vitro assay based on SPA technol. and in an in vitro filtration assay assessing PARP-1 activity (data given). The pharmaceutical composition comprising the compound I is disclosed.

IT 854534-65-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-alkenyl and 6-phenylalkyl substituted 2-quinolinones and 2-quinoxalinones as poly(ADP-ribose) polymerase inhibitors)

RN 854534-65-9 CA

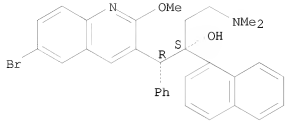
CN 6-Quinolinemethanol, α-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-ethyl-2-methoxy-α-[2-(1-piperidinyl)ethyl]- (CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 64 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 142:211496 CA
TITLE: A Diarylquinoline Drug Active on the ATP Synthase of Mycobacterium tuberculosis
AUTHOR(S): Andries, Koen; Verhasselt, Peter; Guillemont, Jerome; Goehlmann, Hinrich W. H.; Neefs, Jean-Marc; Winkler, Hans; Van Gestel, Jef; Timmerman, Philip; Zhu, Min; Lee, Ennis; Williams, Peter; de Chaffoy, Didier; Huitric, Emma; Hoffner, Sven; Cambau, Emmanuelle; Truffot-Pernot, Chantal; Lounis, Nacer; Jarlier, Vincent
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research and Development, Beerse, 2340, Belg.
SOURCE: Science (Washington, DC, United States) (2005), 307(5707), 223-227
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The incidence of tuberculosis has been increasing substantially on a worldwide basis over the past decade, but no tuberculosis-specific drugs have been discovered in 40 years. We identified a diarylquinoline, R207910, that potently inhibits both drug-sensitive and drug-resistant Mycobacterium tuberculosis in vitro (min. inhibitory concentration 0.06 μg/mL). In mice, R207910 exceeded the bactericidal activities of isoniazid and rifampin by at least 1 log unit. Substitution of drugs included in the World Health Organization's first-line tuberculosis treatment regimen (rifampin, isoniazid, and pyrazinamide) with R207910 accelerated bactericidal activity, leading to complete culture conversion after 2 mo of treatment in some combinations. A single dose of R207910 inhibited mycobacterial growth for 1 wk. Plasma levels associated with efficacy in mice were well tolerated in healthy human volunteers. Mutants selected in vitro suggest that the drug targets the proton pump of ATP (ATP) synthase.
IT 843663-66-1, R 207910
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diarylquinoline drug active on ATP synthase of Mycobacterium tuberculosis)
RN 843663-66-1 CA
CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α-1-naphthalenyl-β-phenyl-, (αS,βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 209 THERE ARE 209 CAPLUS RECORDS THAT CITE THIS RECORD (211 CITINGS)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 65 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 140:163715 CA
TITLE: Preparation of quinoline derivatives and their use as mycobacterial inhibitors
INVENTOR(S): Guillemont, Jerome Emile Georges; Van Gestel, Jozef Frans Elisabetha; Venet, Marc Gaston; Poignet, Herve Jean Joseph; Decrane, Laurence Francoise Bernadette; Vernier, Daniel F. J.
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011436	A1	20040205	WO 2003-EP50322	20030718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493225	A1	20040205	CA 2003-2493225	20030718
AU 2003262529	A1	20040216	AU 2003-262529	20030718
EP 1527050	A1	20050504	EP 2003-771115	20030718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012927	A	20050712	BR 2003-12927	20030718
CN 1671667	A	20050921	CN 2003-817713	20030718
CN 1325475	C	20070711		
NZ 538391	A	20051028	NZ 2003-538391	20030718
JP 2006504658	T	20060209	JP 2004-523812	20030718
CN 101070304	A	20071114	CN 2007-10104947	20030718

US 20050148581	A1	20050707	US 2004-7026		20041208
US 7498343	B2	20090303			
IN 2005DN00220	A	20090313	IN 2005-DN220		20050120
ZA 2005000680	A	20060830	ZA 2005-680		20050124
MX 2005001052	A	20050408	MX 2005-1052		20050125
NO 20050000476	A	20050127	NO 2005-476		20050127
HK 1083496	A1	20080215	HK 2006-103424		20060317
PRIORITY APPLN. INFO.:			US 2002-398711P	P	20020725
			CN 2003-817713	A3	20030718
			WO 2003-EP50322	W	20030718

OTHER SOURCE(S): MARPAT 140:163715
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

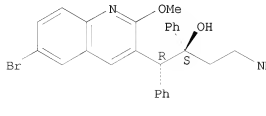
AB The title compds. [I or II; R1 = H, halo, haloalkyl, CN, etc.; p = 0-4; R2 = H, OH, thio, alkoxy, etc.; R3 = alkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl; q = 0-4; R4, R5 = H, alkyl, CH2Ph; or NR4R5 = pyrrolidinyl, imidazolyl, triazolyl, etc.; R6 = H, halo, haloalkyl, etc.; or two vicinal R6 may be taken together to form C:CC:C; r = 0-5; R7 = H, alkyl, aryl, heteroaryl; R8 = H, alkyl; R9 = oxo; or R8 and R9 together form NCH:CH] which are useful for the treatment of mycobacterial diseases, particularly those diseases caused by pathogenic mycobacteria such as Mycobacterium tuberculosis, M. bovis, M. avium and M. marinum, were prepared In particular, compds. are claimed in which, independently from each other, R1 = Br, p = 1, R2 = alkyloxy, R3 = (un)substituted naphthyl or Ph, q = 1, R4 and R5 each independently = H, Me or Et, R6 = H, r = 0-1 and R7 = H. E.g., a multi-step synthesis of III which showed MIC of 0.34 μg/mL and pIC50 of 8.5 against M. tuberculosis and M. smegmatis, resp., was given. Also claimed is a composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of the claimed compds. I, the use of the claimed compds. or comps. for the manufacture of a medicament for the treatment of mycobacterial diseases and a process for preparing the claimed compds.

IT 654653-59-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of quinolines as mycobacterial inhibitors)

RN 654653-59-5 CA

CN 3-Quinolineethanol, 6-bromo-α-[2-(dimethylamino)ethyl]-2-methoxy-α,β-diphenyl-, (αR,βS)-rel- (CA INDEX NAME)

Relative stereochemistry.

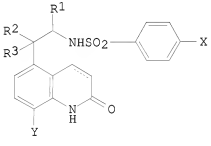


OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (34 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 66 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 119:271031 CA
ORIGINAL REFERENCE NO.: 119:48500h,48501a
TITLE: Preparation of carbostyryls as TXA2 antagonists
INVENTOR(S): Yoshida, Seishi; Yamaji, Yoshiaki; Shinozaki, Katsuo; Jin, Hiromasa; Sato, Hiroki
PATENT ASSIGNEE(S): Zeria Pharm Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05194404	A	19930803	JP 1992-29933	19920122

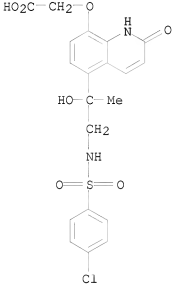
PRIORITY APPLN. INFO.: JP 1992-29933 19920122
OTHER SOURCE(S): MARPAT 119:271031
GI



I

AB Carbostyryls I (R1 = H, lower alkyl; R2, R3 = H, OH, lower alkyl; R2R3 may be O; X = H, halo; Y = CH2CO2H, OCH2CO2H; the dotted line may be double bond) or their pharmacol. acceptable salts, useful as antithrombotics, antiasthmatics, anti-inflammatory agents, antihypertensives, antiarteriosclerotics, etc., are prepared Deprotection of Et [5-[2-(tert-butoxycarbonylamino)ethyl]carbostyryl-8-yl]oxyacetate with CF3CO2H in CH2Cl2 at 0° for 5 h and successive condensation with 4-chlorobenzenesulfonyl chloride in H2O-CH2Cl2 mixture at room temperature for 1 h gave 71% Et [5-[2-(4-chlorobenzenesulfonylamino)ethyl]carbostyryl-8-yl]oxyacetate, which was hydrolyzed with 5N NaOH in MeOH at room temperature for 1 h to afford 96% corresponding carboxylic acid (II). II inhibited blood platelet aggregation at pIC50 7.62, vs. 6.38, for 4-[2-(4-chlorobenzenesulfonylamino)ethyl]phenylacetic acid. Granules were manufactured from II 20, lactose 315, corn starch 125, crystalline cellulose 25 g,

and 200 mL 7.5% hydroxypropyl cellulose aqueous solution
IT 151161-99-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as TXA2 antagonist)
RN 151161-99-8 CA
CN Acetic acid, 2-[[5-[2-[[(4-chlorophenyl)sulfonyl]amino]-1-hydroxy-1-methylethyl]-1,2-dihydro-2-oxo-8-quinolinyl]oxy]- (CA INDEX NAME)

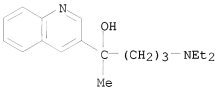


L8 ANSWER 67 OF 67 CA COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 76:94453 CA
ORIGINAL REFERENCE NO.: 76:15144h,15145a
TITLE: Potential antimalarials. 6. 2-Phenyl-6- and -8-quinolinemethanols and 8-phenyl-4-quinolinemethanols
AUTHOR(S): Wommack, J. B., Jr.; Barbee, T. G., Jr.; Subbaswami, K. N.; Pearson, D. E.
CORPORATE SOURCE: Dep. Chem., Vanderbilt Univ., Nashville, TN, USA
SOURCE: Journal of Medicinal Chemistry (1971), 14(12), 1218-20
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 6-Bromo-4-(2-dibutylamino-1-hydroxyethyl)-8-phenylquinoline (I) [34332-13-3] (80-640 mg/kg) showed promising antimalarial activity against Plasmodium berghei. I was nonphototoxic at 50 mg/kg. A series of substituted 2-phenylquinolines had only low activity. To synthesize I, 5-bromo-2-aminobiphenyl-HCl, Me vinyl ketone, and As2O5 were refluxed in EtOH to yield 6-bromo-8-phenylquinoline-4-carboxaldehyde. This was converted with Me2S:CH2 to the 4-epoxyethyl compound, which reacted with Bu2NH to yield I.
IT 35871-06-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 35871-06-8 CA

CN 3-Quinolinemethanol, α-[3-(diethylamino)propyl]-α-methyl-, compd. with 2,4,6-trinitrophenol (1:2) (CA INDEX NAME)

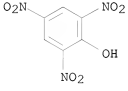
CM 1

CRN 47162-63-0
CMF C18 H26 N2 O



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

=> d his

(FILE 'HOME' ENTERED AT 14:05:20 ON 30 JUL 2009)

FILE 'REGISTRY' ENTERED AT 14:05:34 ON 30 JUL 2009
L1 STRUCTURE UPLOADED
L2 STRUCTURE UPLOADED
L3 STRUCTURE UPLOADED
L4 STRUCTURE UPLOADED
L5 2 S L3 SAM
L6 1 S L4 SAM
L7 974 S L3 OR L4 FULL

FILE 'CA' ENTERED AT 14:09:29 ON 30 JUL 2009
L8 67 S L7

=>

---Logging off of STN---

=>

10/596,270

Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:10:27 ON 30 JUL 2009